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The role of polymerization in adhesive dentistry

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ABSTRACT

Adhesive systems are resin-based materials that reach their final mechanical properties through a polymerization process. Previous literature correlated the failure of the adhesive interface to low polymer setting. Adhesives systems are elaborate mixtures of different molecules of both hydrophilic and hydrophobic nature, included in the formulation to adequately infiltrate the complex dental substrate or added to prolong the stability of the adhesive layer over time. Each adhesive component may influence the polymerization reaction of the material. Photopolymerization is a complex reaction that has several clinical implications, and besides the material composition, it is influenced by multiple factors, including the substrate characteristics, the operator technique, and the light cure unit properties. This review is focused on the analysis of factors that have a potential role in the setting of adhesive materials and thus the ultimate characteristics of the adhesive layer and the stability of the resin-dentin interface.

Contents

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1. Introduction

Adhesive systems significantly revolutionized operative dentistry, allowing dental procedures that were considered unimaginable in the past without creating a retentive cavity and sacrificing sound dental structure. Adhesive systems provide an immediate bond to the tooth substrate, and since the brilliant intuition of Buonocore in 1955 [1] on the application of the acid etching technique to dental enamel, adhesive dentistry has come a long way.

All adhesive systems are resin-based materials able to adhere to enamel and dentin on one side of the interface and to bind to a composite restoration or composite cement on the other side, thanks to a copolymerization process at the adhesive-composite interface. This process is similar for all the adhesive systems, and it allows the sub-optimal polymerized upper layer of the adhesive resin, containing unreacted methacrylate groups (because of the exposure to oxygen, inhibiting the polymerization), reacting with the resin composite [2,3].

Adhesion to enamel and dentin, on the other hand, can be accomplished through two different strategies: the etch-and-rinse technique and the self-etch or etch-and-dry technique [4,5]. In spite of their different approaches, both adhesive strategies rely on the development of micro-retentive resin tags on the enamel substrate and the formation of a hybrid layer or interdiffusion zone (composed of demineralized collagen fibrils immersed in the adhesive resin matrix) at the dentin-adhesive interface [6–8]. The inorganic dentinal matrix is replaced by adhesive monomers that become interlocked between the collagen fibrils after polymerization [9,10]. Besides micro-mechanical retention, some self-etch adhesives with higher pH (mild self-etch adhesives) are also able to chemically interact with the hydroxyapatite calcium covering the collagen in partially demineralized dentin [5,11,12].

Due to the complexity of the dental substrate and the different characteristics of enamel and dentin, dental adhesive systems need to contain different moieties to prepare the substrate and interact with the different components of the tooth surface, because hydrophobic resin monomers cannot infiltrate hydrophilic dental tissues. Thus, adhesive systems must provide demineralization of enamel and dentin, elimination/alteration of the smear layer (depending on the adhesive system strategy) produced during tooth preparation, adequate wettability of the demineralized surface, penetration and infiltration of the adhesive monomers into the dental porosities and then adequate curing of the polymer [13]. For these reasons, adhesive systems contain an *acid or etching component*, able to demineralize both enamel and dentin; a *primer*, which is a compound containing amphiphilic molecules (i.e. with both hydrophilic and hydrophobic characteristics) and solvents, favoring the infiltration of the hydrophobic adhesive monomers, especially between the dentin collagen fibrils, which are very hydrophilic [4,14,15]. The primer penetrates into the demineralized dentin surface making it more hydrophobic for the bonding resin. The *adhesive* also called the *bonding agent or bonding resin* is based on hydrophobic monomers that infiltrate the demineralized surface [14,15] creating a micro-mechanical interaction with enamel and dentin on one side and able to copolymerize with the composite monomers on the other side. This interaction forms the base of the bonded interface between the tooth and the restorative or luting material [16], which should have characteristics of insolubility and resistance to degradation in the oral environment [17,18]. Typically, these three main components can be used separately (three-step etch-and-rinse adhesives) or mixed together in two products (two-step etch-and-rinse adhesives and two-step self-etch adhesives) or one bottle only (one step self-etch adhesives) [14]. The current demand in dentistry is to simplify adhesive procedures through the reduction of both clinical application time and steps. Following this tendency, universal or multimode adhesives that can be used in self-etch, etch-and-rinse, or selective-etch mode have been recently introduced. They resemble self-etch adhesives in composition as they contain acidic monomers [15] and are characterized by chemical interaction with dentin hydroxyapatite [19–25].

Despite the different adhesive strategies, the number of clinical steps and the variety of commercial products available on the market, all adhesive systems contain similar components. The proportion of the ingredients included in the various adhesive systems is the main aspect responsible for their differences, even though manufacturers usually tend not to divulge the exact composition of the marketed adhesives, especially if they contain patented compounds [13]. Each constituent is added with a specific purpose: adhesive systems are a combination of hydrophilic and hydrophobic resin monomers, solvents, photoinitiators, and in some cases filler particles [13,15] to increase strength and reduce polymerization shrinkage [15]. Other additional molecules may be included, especially to prevent degradation of the adhesive interface and prolong its durability [14,26,27].

Ideally, the adhesive-dentin interface should remain stable over time, guaranteeing adequate bond strength, marginal seal, and clinical durability [28]. It has been estimated that composite restorations have an average lifetime of 6–7.2 years [29–32] and one of the primary reasons for replacement, which has not changed in the last 35 years, is secondary caries [33]. Secondary caries is strongly correlated with a weak adhesive interface and as a matter of fact, all adhesive systems have been shown to be somehow unstable and susceptible to degradation, which may be responsible for partial failure of the bond to the tooth leading to marginal leakage and subsequent loss of retention of the restoration [4,5,27,28,34–39]. A two-fold mechanism is implicated in the adhesive interface degradation, based both on the deterioration of collagen fibers [40,41] and the hydrolysis of the adhesive resin [19,20,25]. The demineralization of the dental substrate produced by the etching procedure which leaves exposed collagen fibrils, as well as the exposure to dentinal fluid and saliva components such as water, enzymes, and acids, are all involved in these degradation mechanisms [14,18,27].

As dental adhesives are resin-based materials that achieve their final properties after the setting of the polymer, a failure of the adhesive layer may be a consequence of inadequate polymerization of the material, and each component added to the resin mixture could potentially influence the polymerization reaction and the ultimate characteristics of the adhesive [13]. Photopolymerization is a clinical procedure that has several implications and is more complex than it seems. If the resin material is not properly cured, poor physical properties will be achieved [42–44]. Adequate polymerization of adhesive resins has been clearly correlated with their stability [45,46]. The mechanical properties of light-cured materials depend on the curing efficiency, which is influenced by several factors, including the characteristics of the material, the operator technique and the quality of the light curing unit [47].

The aim of this paper is to analyze the polymerization of adhesive systems and the role of the different factors that might affect polymer curing, and thus the ultimate stability of the resin–dentin bonds.

2. Monomers and hydrophilicity

Dental adhesives are composed of monomers that are similar to those used in dental composite materials (Table 1), guaranteeing a strong bonding between the adhesive layer and the resin composite. Bisphenol-glycidyl methacrylate (bis-GMA) is the most common monomer used as the bonding component of dental adhesives and has been shown to work as an excellent bonding agent when applied to enamel. However, as the dentin substrate is intrinsically hydrophilic due to its moist nature, very hydrophobic monomers like bis-GMA are not able to infiltrate it well after demineralization [15]. For this reason, more hydrophilic monomers are usually used as primers in dental adhesives to enhance wetting properties. For instance, hydroxylethyl methacrylate (HEMA) is totally miscible in water, and a mixture of Bis-GMA and HEMA is frequently employed in dental adhesive systems to provide intermediate characteristics of hydrophilicity [15,16]. Several other monomers have been included in adhesive systems following the continuous evolution and innovation of materials (Table 1). In general, the hydrophilicity of the polymer can be increased through the addition of functional groups such as ethyl, methyl or hydrogen to replace amide, phosphate, carboxylic and hydroxyl groups and through the incorporation of ether and ester linkages. Monomers characterized by the presence of amino, hydroxyl, alcohol, and acidic moieties are usually added to obtain a chemical interaction with the dentin collagen and hydroxyapatite [15]. However, methacrylate adhesives containing hydrophilic groups, such as urethane, hydroxyl, phosphate, ester, and carboxyl moieties [13], are more susceptible to hydrolysis in the oral environment [48], due to water sorption in the adhesive layer which may behave as a permeable membrane [39,49–52]. A diffusion of water through the loosely cross-linked polymers or hydrophilic regions at the base of the bonded interface [53,54] leads to the formation of channels in the adhesive layer, in which water is able to flow more freely [27], causing a rapid degradation of the hydrophilic domains at the adhesive interface [26,55] and potentially the breakage of ester bonds in the methacrylate resin [17,27,56]. Plasticization and swelling of the adhesive layer induced by water may further increase the penetration of salivary esterases that can accelerate the hydrolytic process, which is considered one of the main reasons for the failure of the hybrid layer over time [26,57]. Resin hydrolysis is also responsible for the exposure of collagen, which is then exposed to the action of proteolytic enzymes of dentinal origin, causing the deterioration of the collagen fibers, the other main process involved in adhesive failure [58–60] compromising the long-term integrity of the bonded interface [14,27,49,51].

The water exchange and hydrolysis can likewise cause leaching of potentially toxic components from the adhesive resin, such as unreacted monomers, free radicals, and photoinitiators. As a consequence, allergic reactions and irritation phenomena involving the tooth pulp and the oral mucosa have been related to the elution of toxic derivatives from the degraded polymers [47,61,62].

Previous studies have demonstrated the presence of permeable microdomains composed of hydrophilic and/or acidic functional groups in the adhesive layer using a silver tracer that is able to reveal the presence of nanoleakage [63]. These silver-infiltrated permeable zones within the resin layer are considered the expression of the hydrolytic process [63], which has been related to a poor polymerization of the adhesive resins [45,46,64,65] (Fig. 1).

Similar to all resin materials, adhesive systems also acquire their final properties through a polymerization process, characterized by the conversion of carbon-carbon double bonds of the monomers into carbon–carbon single bonds connecting one monomer to another, forming a long chain and interchain crosslinks, which transform the initial monomers into a stiff and strong polymer [15].

In light-curing or photo-curing materials, polymerization can be obtained through the exposure of the adhesive monomers to a photo-curing light of sufficient output and appropriate wavelength, which must match the wavelengths absorbed by the photoinitiator (generally camphorquinone) included in the adhesive for this purpose [66]. As an alternative, typically when light cannot reach the resin monomers, a chemical-activated reaction (self-curing) can be used. A combination of photo and self-curing polymerization is also possible in dual-curing materials [15].

The extent to which the adhesive monomers are converted into a polymer is responsible for the length of the polymer chains, which, in turn, determines the final strength of the polymer [67]. For this reason, adhesives must be properly light-cured following the manufacturer recommendations to obtain a stable bonded interface.

Independent of the adhesive type and the number of steps necessary for its application [27,60], sub-optimal polymerization followed by permeability to water movement [45,46,68], is an issue potentially affecting all types of adhesive systems (Fig. 2), though it is more pronounced in simplified systems (e.g., two-step etch-and-rinse, one-step self-etch systems) due to the inclusion of greater amounts of hydrophilic monomers [45,46,68]. On the contrary, adhesive systems based on solvent-free hydrophobic monomers show a more complete polymerization and lower permeability [45]. Two-step etch-and-rinse adhesives are characterized by sub-optimal polymerization and increased permeability, which leads to water sorption, reduced mechanical properties [69] and increased nanoleakage [50,55,70]. One-step self-etching adhesives in their initial formulation, have also been shown to be less polymerized than multistep adhesive systems, thus showing increased permeability [45,46]. Acidic monomers of self-etch adhesives may chemically react

Table 1 – Abbreviations and molecular structure of main components used in adhesives.

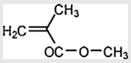
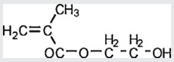
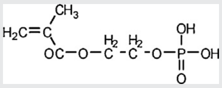
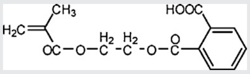
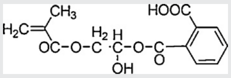
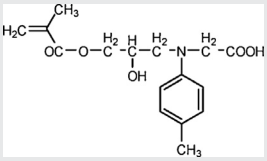
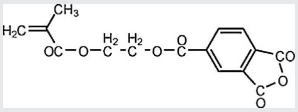
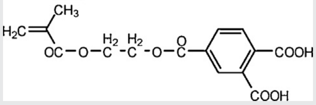
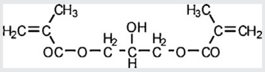
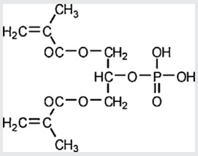
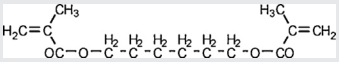
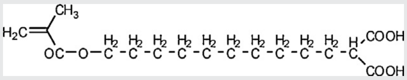
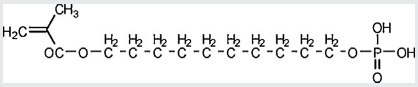
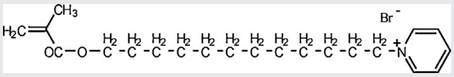
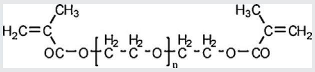
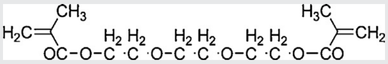
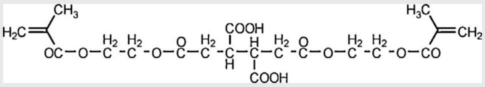
Monomers	Structural formula
MMA Methyl methacrylate	
HEMA 2-Hydroxyethyl methacrylate	
HEMA-phosphate 2-Hydroxyethyl methacrylate phosphate	
MMEP Mono-2-methacryloyloxyethyl phthalate (sometimes also called PAMA: phthalic acid monomethacrylate)	
PAMM Mono(2-methacryloxy-1-hydroxy)ethyl phthalate	
NGT-GMA *N*-Tolylglycine glycidyl methacrylate or *N*-(2-hydroxy-3-((2-methyl-1-oxo-2-propenyl)oxy)propyl)-*N*-tolyl glycine	
4-META 4-Methacryloyloxyethyl trimellitic anhydride	
4-MET 4-Methacryloyloxyethyl trimellitic acid	
GDMA Glycerol dimethacrylate	
GPDM Glycerolphosphoric acid dimethacrylate	
HDDMA 1,6-Hexanediol dimethacrylate	
MAC-10 11-Methacryloyloxy-1,1-undecane dicarboxylic acid	
10-MDP 10-Methacryloyloxydecyl dihydrogen phosphate	
MDPB: Methacryloyloxydodecyl pyridinium bromide	
PEGDMA Polyethylene glycol dimethacrylate	
TEGDMA Triethylenglycol dimethacrylate	
TCB Butan-1,2,3,4-tetracarboxylic acid di-2-hydroxyethylmethacrylate ester	

Table 1 (Continued)

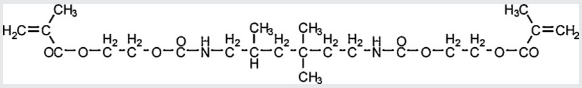
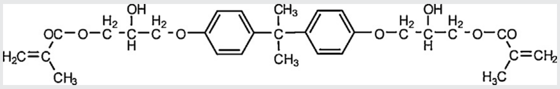
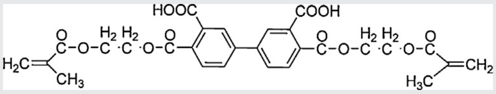
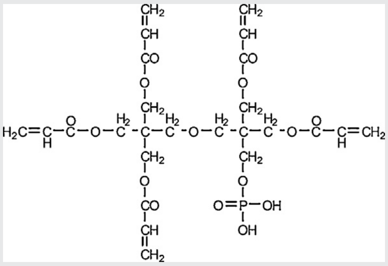
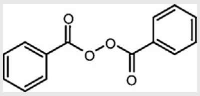
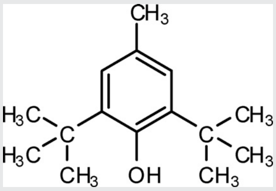
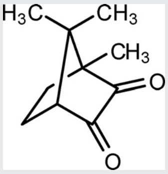
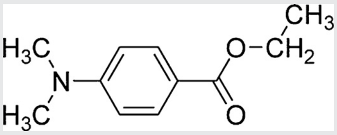
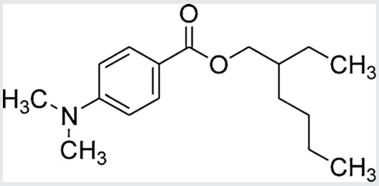
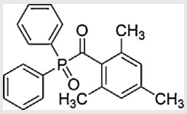
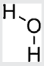
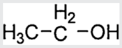
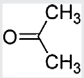
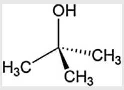
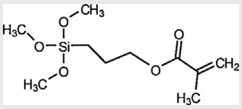
UDMA Urethane dimethacrylate or 1,6-di(methacryloyloxyethylcarbamoyl)-3,3,5-trimethylhexane	
Bis-GMA 2,2-Bis[4-(2-hydroxy-3-methacryloyloxypropoxy)phenyl] propane	
BPDM Biphenyl dimethacrylate or 4,4′-dimethacryloyloxyethyl oxycarbonyl biphenyl-3,3′-dicarboxylic acid	
PENTA Dipentaerythritol pentaacrylate monophosphate	
Initiators and inhibitors	Structural formula
BPO Benzoylperoxide (redox initiator)	
BHT Butylhydroxytoluene or butylated hydroxytoluene or 2,6-di-(tert-butyl)-4-methylphenol (inhibitor)	
CQ Camphorquinone or 1,7,7-trimethylbicyclo-[2.2.1]-hepta-2,3-dione (photo-initiator)	
EDMAB Ethyl 4-dimethylaminobenzoate (co-initiator)	
ODMAB 2-(Ethylhexyl)-4-(dimethylamino) benzoate (co-initiator)	
TPO Diphenyl(2,4,6-trimethylbenzoyl)-phosphine oxide (photo-initiator)	
Solvents	Structural formula
H_2O Dihydrogen oxide or water	

Table 1 (Continued)

EtOH Ethanol or ethyl hydroxide	 $H_3C{-}\overset{H_2}{C}{-}OH$
ACETONE (CH_3COCH_3) Acetone or dimethyl ketone or propanone	
TBA Tert-butyl alcohol, tert-butanol	
Additives and silane coupling agents	Structural formula
Coupling agent A174 Methacryloxypropyltrimethoxysilane	
NaF Sodium fluoride	 $\overset{\oplus}{Na}\ \overset{\ominus}{F}$

with hydroxyapatite [71]. Dissolved hydroxyapatite should behave as a buffer [72,73], reducing the interference with polymerization caused by a highly acidic pH [72,74,75]. The acidity of self-etching adhesives, however, will probably not be completely buffered from the demineralized hydroxyapatite, resulting in continued etching [76] and sub-optimal polymerization [45,76]. Self-etch adhesives are also characterized by a high hydrophilic-monomer content, contributing to the increased permeability of the hybrid layer to water movement [51,77,78], and leading to hydrolytic degradation phenomena [17,27,37]. Hydrophobic monomers have been included in one-step adhesives to obtain more stable polymers, but hydrophilic monomers tend to cluster prior to the polymerization reaction, forming hydrophilic areas [79,80] and water-filled channels [81] that allow water infiltration from the dentin through the hybrid layer [51,63], ultimately turning it into a porous structure with poor sealing ability (Fig. 3).

Water may remain trapped within the adhesive layer during photopolymerization [53,54], and its presence at the tooth/adhesive interface may cause a sub-optimal polymerization of the adhesive monomers [82], contributing to increased permeability within the hybrid layer [55]. Moreover, hydrophilic monomers have shown a lower conversion due to adhesive phase separation phenomena [79] and incompatibility between hydrophilic monomers and hydrophobic photoinitiators [83].

The use of a light source with an adequate radiant exitance and using exposure times exceeding those recommended by manufacturers has been shown to improve the degree of conversion and reduce the permeability of simplified adhesives, contributing to enhance their *in vitro* performance [45,46,84]. However, attention should be paid not to cause an excessive temperature increase that can have a harmful effect on the pulp, in particular when high power curing lights are used [85].

Recently, the inclusion of nanogel additives in dental adhesives has been proposed to reduce water solubility and improve the longevity of the adhesive layer [86]. Nanogels are functionalized prepolymers in the form of crosslinked globular particles that can be added to resin monomers, such as those used in dental adhesives, without modifying the conventional adhesive application procedure [86]. When the solvent is evaporated, nanogels tend to coalesce, potentially reinforcing the adhesive resin network [86]. The main advantage is that the combination of monomers into macromolecular prepolymer agglomerates reduces phase separation, which is a desirable property when working on hydrophilic surfaces [87]. Moreover, nanogel particles do not tend to leach from the polymer network [88], thus producing a more stable adhesive interface.

Preliminary studies investigated different nanogel combinations in experimental bonding systems, reporting the mechanical reinforcement of the adhesives without impairing their degree of conversion and solvent evaporation [86], and with a viscosity of the tested materials similar to that of conventional adhesives [87]. Moreover, the microtensile bond strength of nanogel-based adhesives seemed to be improved in the short term [86]. Further research is necessary to identify the optimal combinations, because the effect of the inclusion of nanogel particles was related to their hydrophilic/hydrophobic nature: the more hydrophobic nanogels lead to increased mechanical properties, while the hydrophilic ones provided the highest dentin bond strength values [88].

3. Photoinitiators

During the polymerization reaction, hydrophilic and hydrophobic monomers should adequately cross-link to obtain a strong adhesive layer [89]. Nevertheless, the concurrent presence of hydrophilic and hydrophobic domains has been frequently associated with nano-phase separation phenomena, especially in simplified adhesives [90,91], leading to the development of non-homogeneous adhesive layers. Camphorquinone (CQ), the most common photo-initiator in adhesive systems, has a hydrophobic nature, and may not provide for optimal conversion of the hydrophilic monomers [92].

Moreover, in self-etch adhesives, the degree of conversion of systems based on CQ is negatively influenced by acidic functional monomers, which inactivate the required amine co-initiator through an acid-base reaction [75,93].

For this reason, the use of alternative hydrophilic photoinitiators, besides conventional CQ-amine systems, has been proposed [92,94]. Systems based on Norrish type I initiators, such as acyl phosphonates, acylphosphine oxides

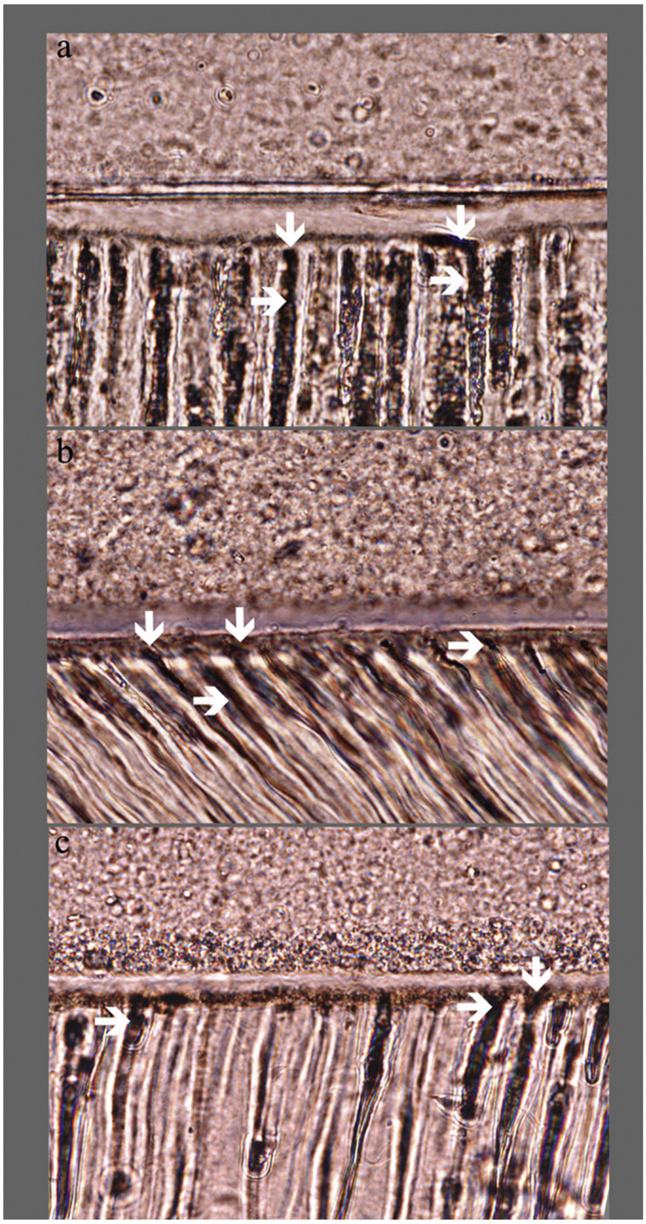


Fig. 1 – Light micrographs showing representative views of nanoleakage interfacial expression along the hybrid layers created by one-step self-etch adhesives. (a) Adhesive interface produced by AdheSE One showing the highest nanoleakage expression (arrows). (b–c) Adhesive interfaces created by Adper Prompt L-Pop (b) and iBond (c), showing minor silver deposits (arrows) mainly localized at the bottom of the hybrid layer.
Reproduced from Navarra et al., Eur J Oral Sci 2009; 117: 463–469, with permission.

and bisacylphosphine oxides [95,96] have all been proposed. Among these, TPO (ethyl 4-dimethylaminobenzoate and diphenyl(2,4,6-trimethylbenzoyl)-phosphine oxide) has become a popular alternative initiator to improve the DC of hydrophilic adhesive systems [89,92,94]. Indeed, the addition of a water-compatible initiator reduced the phase separation phenomena [91] and improved the stability of the adhesives by increasing the polymerization of both hydrophilic and hydrophobic domains [89] (Fig. 4). Using a mini-interfacial fracture toughness (mini-iFT) test [71], the effect of TPO compared to CQ on the DC and mechanical properties of an experimental one-step self-etch adhesive formulation was evaluated. TPO increased the DC of the tested adhesive, but did not show a significant dark cure reaction when compared to the CQ-based adhesives [71,97]. Also, bis(acyl)phosphine oxide (BAPO) and phenylpropanedione (PPD) photoinitiators have been shown to improve the DC of adhesive systems compared to CQ [98–100].

Recently, a borate system (BO) [101] has been proposed in a commercial one-step self-etch adhesive (One-Up Bond F Plus — Tokuyama Dental). The exact mechanism of action of BO is not well clarified [102–104], however, in experimental conditions, BO leads to a high degree of conversion values.

It is evident that the degree of conversion of adhesives is influenced by the constituent functional monomers. Thus, the photo-initiator system should be selected according to adhesive system formulation, considering the presence of hydrophilic domains and solvents, avoiding potential conflicts between the adhesive components and the photo-initiator system [101]. Hydrophilic photoinitiators should be included within the simplified adhesive formulations to ensure an adequate DC at the adhesive interface and reduce degradation phenomena.

4. Solvents

Besides hydrophilic monomers, the priming components of adhesive systems contain organic solvents to increase the wettability and the infiltration of the adhesive resins into the dentin substrate. Also, systems that combine primer and bonding resins in the same mixture contain high percentages (up to 50%) of solvents [13]. The most commonly used solvents are water, ethanol, and acetone. They serve as diluting agents of the resin mixture [27]. Ethanol and water are very hydrophilic and promote the interaction between monomers and dentinal water. In contrast, acetone acts by removing water from the dentin [15]. After application, any solvent must be adequately air-dried in order to be displaced from the adhesive mixture [15]. Any residual solvent not properly evaporated prior to polymerization will remain integrated within the adhesive layer [105]. As solvents used in adhesive dentistry are not polymerizable molecules and cannot form networks with the adhesive monomers, they may interfere with adhesive polymerization and act as plasticizing agents, weakening the polymer structure and reducing the physical properties of the adhesive resin [15,84].

On the other hand, solvents decrease adhesive viscosity, improving the infiltration of resin into demineralized dentin and the mobility of monomers and growing polymer chains [84,106,107]. Up to a certain degree, solvents can promote the extent of cross-linking, but at higher concentrations, the degree of conversion is reduced because of the increase of the distance between radicals during the polymerization reaction [108]. Previous studies demonstrated that when adhesive systems contain high solvent concentrations before photo-curing, lower degrees of conversion are obtained [84]. Indeed,

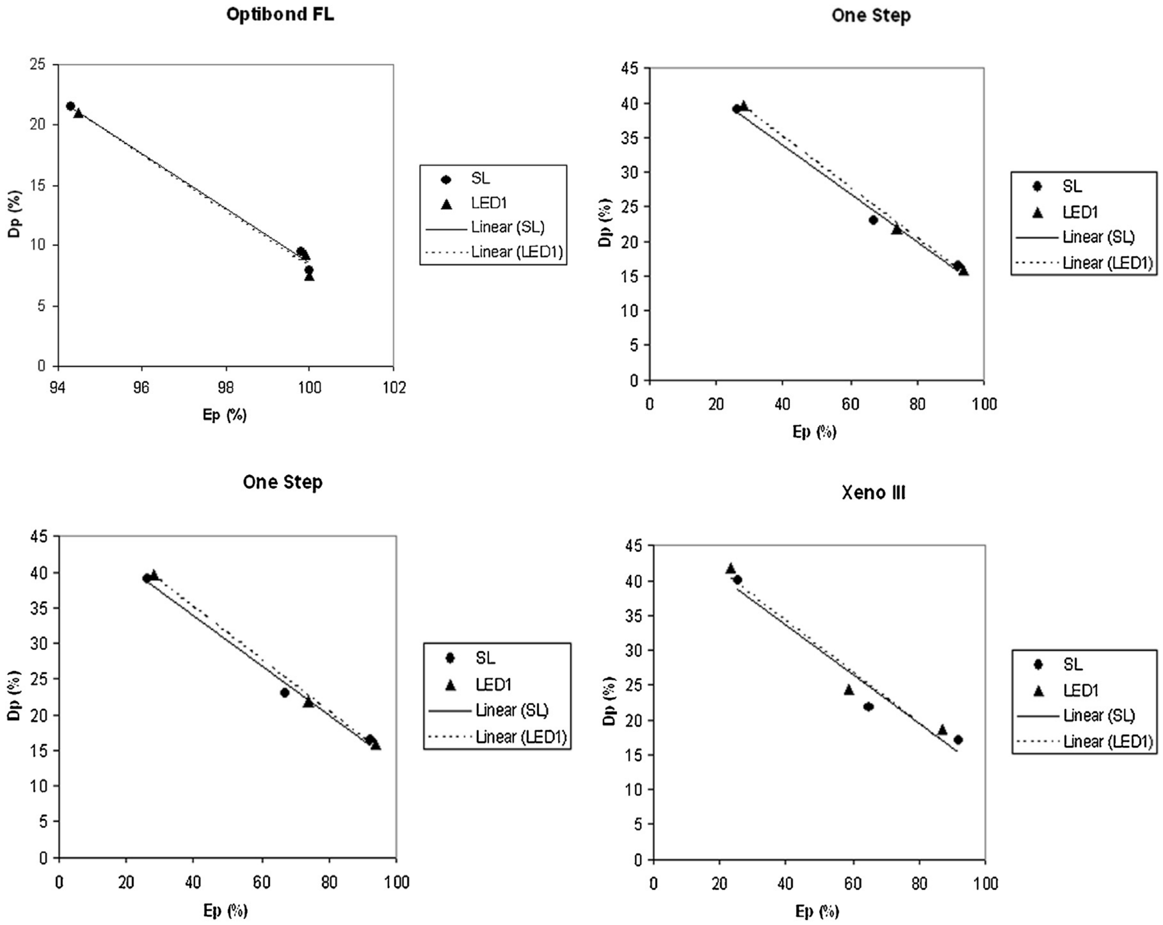


Fig. 2 – Significant inverse correlations ($p < 0.05$) between permeability and extent of polymerization (Ep%) for four exemplifying adhesives.
Reproduced from Breschi et al., Dent Mater 2007; 23(9):1066–1072, with permission.

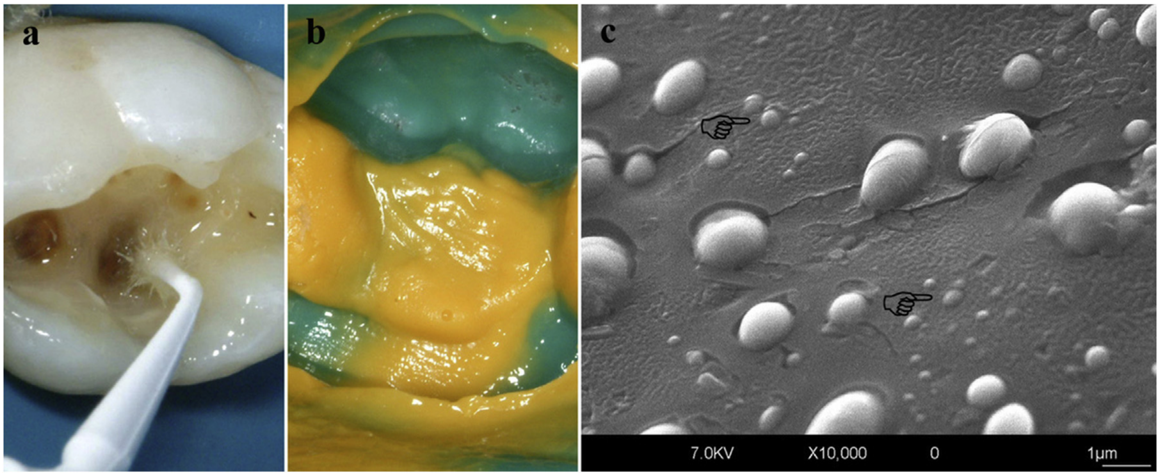


Fig. 3 – Illustrative steps of the in vivo analysis of the permeability of adhesives in accordance with Chersoni et al. [51]. A cavity was prepared and bonded (a), and an impression of the cavity floor was obtained (b). After pouring a cast with epoxy resin, specimens analyzed under FEI-SEM revealed water droplets emanating from the adhesive surface (c). These droplets are the morphological evidence of water that seeped from the adhesive layer during the setting time of the hydrophobic impression material forming major droplets as well as minor droplets (pointing finger) over the adhesive.
Reproduced from Breschi et al., Dent Mater 2008;24(1):90–101, with permission.

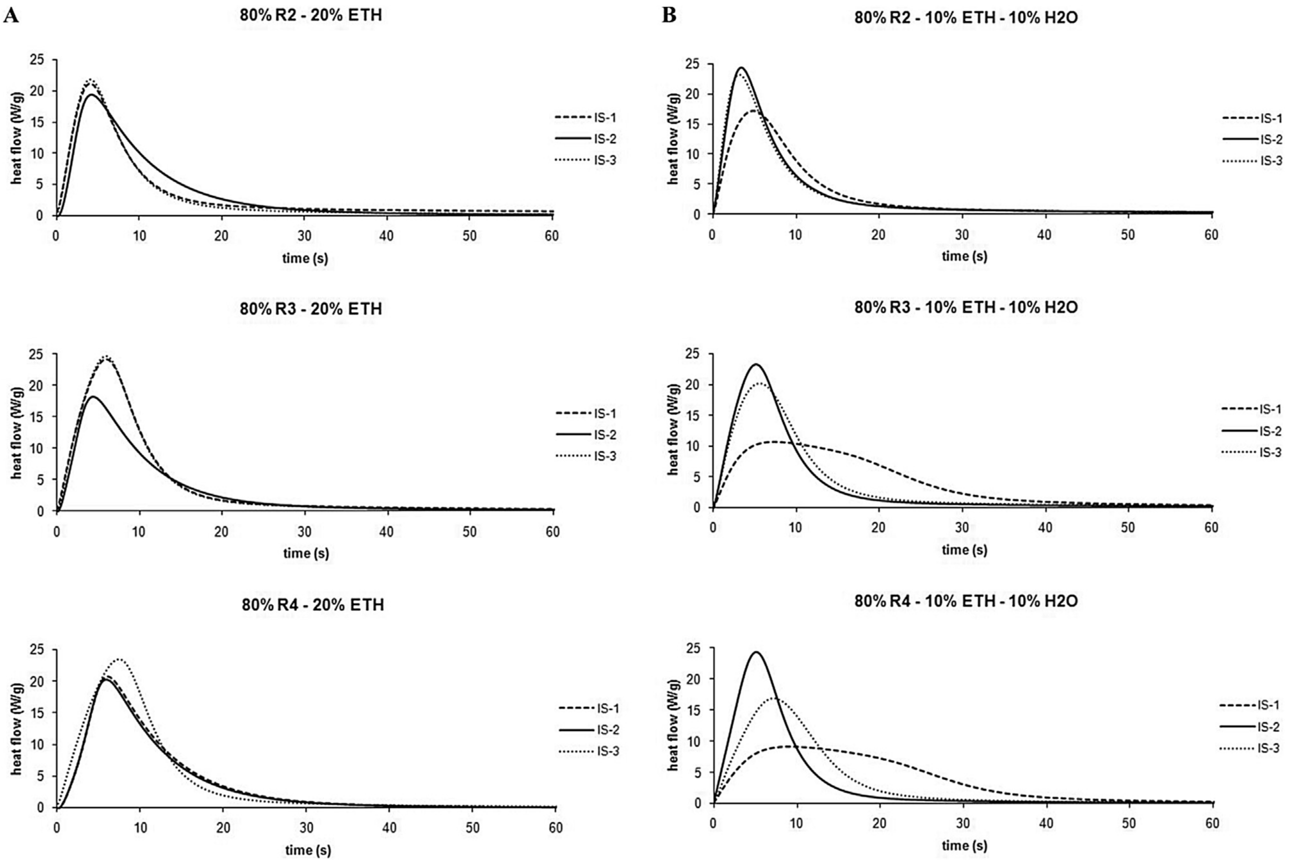


Fig. 4 – (A–B) Representative DSC curves of adhesive resin mixtures solvated with 20% ethanol or 10% ethanol and 10% water tested with different initiators systems: R2 (more hydrophobic) was the less affected by the presence of water compared to R3 and R4 (more hydrophilic) that showed a smaller and broader peak related to the slower speed of reaction if TPO (IS-1) was used.
Reproduced from Cadenaro et al., Dent Mater 2010;26(4): 288–294, with permission.

the ideal solvent concentration for optimal polymerization is higher than the optimal solvent concentration for physical properties of adhesive resins [108], as the highest mechanical properties of adhesives are achieved by polymerization of unsolvated comonomers [108–110]. Thus, there are opposite trends in adhesive dentistry: for instance, a 10–20% residual ethanol in the resin mixture prior to light-curing can be useful to increase the degree of conversion, but this solvent concentration reduces the physical properties of the polymer [84] (Table 2). Lower mechanical properties of adhesive polymers have been previously associated with higher solvent content [111,112].

Residual water may also cause phase separation of hydrophobic and hydrophilic groups in the adhesive mixture [79], adversely affecting the curing reaction by hampering the development of adequately cured polymers within the adhesive layer [92,109]. Thus, solvent evaporation is mandatory before polymerization and should be performed thoroughly to allow the monomers to remain close enough to react efficiently and to prevent the softening of the final polymer by the residual solvent.

Nonvolatile monomers with relatively low vapor pressure when mixed with solvents (e.g., water) reduce the solvent evaporation ability in relation to the monomer concentration, as expressed by Raoult's law [113]. This means that in water–monomer mixtures, complete water evaporation is not possible [113]. The same scenario also occurs in ethanol- and acetone-based resin mixtures; in clinical conditions, as the solvent gradually evaporates, the relative nonvolatile monomer concentration rises, decreasing the vapor pressure of the residual solvent and impeding complete solvent evaporation [84]. For this reason, the optimal solvent concentration must be determined for each adhesive formulation in relation to the resin composition and solvent type. Even though a complete removal of the solvent is impossible, the evaporation should be maximized, and the adhesive layer must be thoroughly and repeatedly air-dried to ensure adequate solvent evaporation [114]. Manufacturers recommend air-drying times of 5–10 s, not because it assures the most optimal evaporation, but because they want to offer user-friendly products that are considerate of the practitioner's time [84]. Bond strength and hybrid-layer homogeneity may be further improved applying a warm, dry air-stream to evaporate the solvent following the application of the primer or primer & bonding solution [115].

Independent of the type of solvent used, sufficient adhesive polymerization is necessary to compensate for the negative effects of low solvent evaporation [3,108]. Increasing the exposure time beyond those recommended by manufacturers can

Table 2 – Percent monomer conversion (DC) (mean ± SD) values for five experimental resins and their respective resin/ethanol mixtures (% comonomer/%EtOH), at different exposure durations.

Resin 1	DC at 20 s	DC at 40 s	DC at 60 s
Neat	46.7 ± 1.1^{CD}	53.3 ± 1.2^{EF}	56.4 ± 1.5^{F}
90/10	41.2 ± 1.0^{ABC}	51.7 ± 1.1^{EF}	53.5 ± 1.0^{EF}
80/20	33.3 ± 1.1^{AB}	45.2 ± 0.5^{CDE}	$49.8 \pm 1.0C^{DEF}$
70/30	26.3 ± 1.7^{AB}	41.3 ± 0.5^{BCD}	$48.3 \pm 0.6C^{DE}$
Resin 2	DC at 20 s	DC at 40 s	DC at 60 s
Neat	50.4 ± 0.4^{A}	54.1 ± 0.2^{B}	55.5 ± 0.3^{B}
90/10	63.7 ± 0.8^{C}	68.2 ± 0.3^{D}	70.2 ± 0.4^{E}
80/20	66.6 ± 0.8^{D}	75.2 ± 0.7^{F}	79.8 ± 0.6^{G}
70/30	51.0 ± 2.6^{A}	75.0 ± 0.2^{F}	81.5 ± 0.2^{G}
Resin 3	DC at 20 s	DC at 40 s	DC at 60 s
Neat	53.0 ± 0.4^{B}	57.0 ± 0.6^{C}	58.4 ± 0.2^{C}
90/10	69.5 ± 0.3^{E}	72.2 ± 1.1^{E}	74.9 ± 0.7^{E}
80/20	65.5 ± 1.2^{D}	82.7 ± 0.4^{G}	86.3 ± 0.3^{H}
70/30	39.7 ± 1.9^{A}	78.1 ± 1.1^{F}	88.8 ± 0.3^{H}
Resin 4	DC at 20 s	DC at 40 s	DC at 60 s
Neat	55.5 ± 0.4^{B}	59.3 ± 0.2^{C}	61.2 ± 0.3^{C}
90/10	68.8 ± 0.7^{E}	74.6 ± 0.4^{F}	76.8 ± 0.5^{G}
80/20	61.0 ± 0.6^{C}	82.2 ± 0.2^{H}	86.0 ± 0.4^{I}
70/30	30.4 ± 1.1^{A}	63.8 ± 1.1^{D}	83.5 ± 0.8^{H}
Resin 5	DC at 20 s	DC at 40 s	DC at 60 s
Neat	55.5 ± 0.4^{B}	60.9 ± 0.5^{C}	63.6 ± 0.3^{CD}
90/10	74.4 ± 0.6^{F}	82.3 ± 0.6^{G}	84.1 ± 0.4^{GH}
80/20	67.6 ± 1.0^{DE}	86.1 ± 0.9^{GH}	87.9 ± 3.3^{H}
70/30	41.2 ± 0.9^{A}	71.8 ± 5.9^{EF}	85.2 ± 0.5^{GH}

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The DC% values are expressed as mean values ± standard deviations. Within any experimental resin system means followed by the same superscript letter indicate no difference ($p < 0.05$) among each resin. 90 res/10 et refers to 90 mass% resin/10 mass% ethanol. N = 5 specimens per group. 90 resin/10et indicates 90 wt% resin/10 wt% ethanol.

improve the degree of conversion and reduce adhesive permeability, even in the presence of residual solvent [84,116,117].

5. The influence of MMPs inhibitors on adhesives polymerization

Since neither E&R nor SE adhesives can fully penetrate the dentin collagen network, denuded collagen fibrils surrounded by water are always present on the bottom of the hybrid layer after the bonding procedures, and this is the weak area of any resin-dentin interface [118–120]. In the demineralized dentin, endogenous proteases, mainly matrix metalloproteases (MMPs) and cysteine cathepsins, are reactivated [18,121–123], and in the presence of water, they can hydrolyze collagen fibers [59]. MMPs are proteases dependent on zinc and calcium ions to maintain their active state. The true collagenases, MMP-1, −8, −13 and −18, are responsible for collagen degradation [124]. However, they cannot initially bind the collagen triple helix since the binding position is protected by C-telopeptides, making the collagen triple helix structurally positioned in such a way that the large collagenase molecule cannot fit [125]. Hence, removing the protective telopeptides is the key factor which facilitates the unwinding of the triple helix and the collagenolytic activity of true collagenases [126]. The telopeptidases which enable this process are MMP-2 and −9 [125]. Therefore, inhibition/inactivation of the MMPs is considered a very important strategy for the preservation of the hybrid layer [14,127].

There have been numerous reports on the beneficial effect of protease inhibitors on the longevity of the hybrid layer [128–134]. Primarily, agents that are able to influence the activity of endogenous dentinal enzymes can be enzyme inhibitors, and collagen cross-linkers. The most extensively investigated inhibitor is chlorhexidine (CHX) [130,131,135–141], an antimicrobial agent with broad use in dentistry, characterized by excellent substantivity both on mineralized and demineralized dentin [142,143], and able to inhibit MMPs in very low concentrations due to its chelating properties [144]. Another group of inhibiting agents are the quaternary ammonium methacrylates (QAMs), which are cationic antimicrobial molecules, which in certain cases also demonstrate anti-MMP properties [145–147]. Methacryloyloxydodecylpyridinium bromide (MDPB) is an example of a QAM that has already been incorporated into a commercial adhesive system (Clearfil Protect Bond, Kuraray Noritake Dental Inc., Osaka, Japan) [148,149]. The advantage of MDBP is that it can copolymerize with methacrylates in the adhesive resin, thereby keeping it from being leached from the adhesive and serving as a contact-kill agent for microbes [150,151]. Tetracycline and its analogs (doxycycline and minocycline) also exhibit protease-inhibitory properties [152–154].

On the other hand, the ability of cross-linkers to preserve the hybrid layer can be attributed to several mechanisms. First, they are reported to reinforce the collagen structure by making additional cross-links between the collagen molecules, making them less prone to hydrolysis. Second, they can also cross-link MMPs and inactivate them by changing their molecular mobility, further disabling the degeneration process [155–157]. For instance, aldehydes, such as glutaraldehyde and acrolein are very strong cross-linkers, but are perhaps less convenient for clinical use due to their potential cytotoxicity [158,159]. Therefore, agents with low cytotoxicity, such as carbodiimides [133,160–163], and natural cross-linkers, such as proanthocyanidin extracted from grape seeds [134,164,165], have been extensively investigated. Due to their efficacy and biocompatibility, they may more appropriate candidates for clinical use.

These inhibitors and cross-linkers have been initially tested as separate primers in aqueous solutions and have shown promising results [132,135,146,158,160]. However, in accordance with the current tendency to simplify and reduce the number of steps in the adhesive procedure, there have been efforts to incorporate these agents into one of the components of the adhesive system. Further, while cross-linkers are thought to permanently inactivate the MMPS, the effect of inhibitors could be reversible, since they could leach out of the hybrid layer, given their solubility in water (CHX) [166,167]. Hence, another reason for putting the inhibitor into the adhesive is to make it available for slow release from the adhesive to prolong its activity and preserve the hybrid layer over a longer period of time.

Table 3 – Changes in degree of conversion (DC) and modulus of elasticity (E) of experimental resins of increasing hydrophilicity added with different concentrations of CHX.

		DC (%)	E modulus (MPa)
R2	Neat resin	60.81 (0.48)^{b}	908.59 (30.68)^{C}
	1% CHX	60.22 (0.17)^{b}	1068.37 (8.48)^{B}
R3	Neat resin	64.44 (0.47)^{c}	1383.10 (21.26)^{A}
	1% CHX	64.64 (0.68)^{c}	762.01 (1.50)^{E}
	5% CHX	59.96 (0.43)^{b}	724.66 (16.69)^{D}
R4	Neat resin	67.71 (0.71)^{d}	843.25 (1.68)^{D}
	1% CHX	70.17 (0.66)^{e}	648.57 (2.49)^{F}
	5% CHX	70.95 (0.87)^{e}	621.37 (6.07)^{D}
R5	Neat resin	56.08 (0.67)^{a}	640.10 (8.60)^{F}
	1% CHX	60.32 (0.53)^{b}	372.55 (2.12)^{H}
	5% CHX	59.79 (0.57)^{b}	346.93 (24.03)^{H}

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Values are expressed as Mean (±SD). Different superscript lower case letters indicate statistical differences between the groups for DC ($p < 0.05$) n = 10/group. Different superscript upper case indicate statistical differences between the groups for E modulus ($p < 0.05$). n = 10/group. CHX = chlorhexidine.

Inhibitors and cross-linkers have been blended into experimental and commercially available etchants, primers, or adhesive resins, yielding mixed results. There are various risks related to adding a new component into a stable system, since there could be repercussions on the quality of polymerization and mechanical properties of the adhesive. A recent study [168] found no adverse effects of the incorporation of CHX digluconate (0.5, 2 and 4 wt%) into an experimental E&R adhesive on the degree of conversion (DC). Cadenaro et al. [169] also found that the incorporation of 1% or 5% CHX within resin blends of increasing hydrophilicity did not affect DC, but it decreased the elastic modulus significantly (Table 3), which stresses the need for comprehensive investigation of different mechanical properties of experimental adhesives before consideration for clinical use. CHX was further reported not to adversely affect DC, water sorption, ultimate tensile strength or solubility of an E&R adhesive, while preserving bond strength for 12 months [170]. Da Silva et al. [171] tested experimental E&R adhesives doped with several inhibitors: Galardin, Batimastat, GM1489, and CHX diacetate and showed similar results with CHX and GM1489. Moreover, although five different QAM-containing adhesive blends showed an increase in DC, a decrease in Young's modulus and ultimate tensile strength was observed [147].

Another approach to be considered is the incorporation of the cross-linkers into adhesive blends since they might demonstrate multiple roles in resin-dentin preservation. For instance, quercetin is a flavonoid, an antioxidant with cross-linking properties, known to down-regulate expression of MMP2 and −9 in prostate cancer cells. Gotti et al. [172] and Yang et al. both investigated the incorporation of quercetin into AdperTM Single Bond 2 (3 M ESPE, St. Paul, MN, USA) [172,173], and the former reported lower DC and bond strength in the experimental adhesive blend, while the latter presented a decrease in DC only in the group containing higher concentrations of quercetin, with the preservation of the hybrid layer over time. This discrepancy could be due to the differences in the concentration of the active substance (5 wt% vs. 100/500/1000 μg/mL). Gotti et al. also investigated two other adhesive systems and different antioxidants, and only the Clearfil SE (Kuraray Medical; Tokyo, Japan) presented no impairment of DC in the experimental groups. The high variability in the achieved results leads to the conclusion that the mechanical properties of a certain adhesive blend could be impaired or improved depending on the physicochemical interactions of the components of the adhesive system with a therapeutic compound added in a certain concentration. Hence, efforts should be directed towards matching appropriate inhibitors in adequate concentrations with appropriate adhesive resin blends [174].

Adhesive systems doped with different therapeutic agents could be less dependent on the composition of the adhesive and concentration of the therapeutic agent if certain fillers, serving as carriers of the active substance, could be incorporated within the adhesive. This could have a double impact, since fillers have been shown to improve mechanical properties of adhesives [168], and the addition of an inhibitor/cross-linker would not disturb the balance in the liquid part of the adhesive. Hence, there would be a less potential impact on polymerization quality. Moreover, some of these carriers could be 'programmed' to release inhibitors gradually, ensuring a prolonged inhibitory effect. There have been several reports on such experimental adhesives recently. Bottino et al. [175] first investigated whether incorporation of Halloysite® nanotubes into an adhesive would influence its mechanical properties. They found no differences in DC, microhardness and bond strength compared to the control when 20 wt% of nanotubes were added. Further, the same group investigated whether encapsulation of doxycycline into the nanotubes would cause changes in DC and microtensile bond strength, but the system remained stable [176]. Most recently, the authors loaded doxycycline into Halloysite® nanotubes and performed a comprehensive investigation of the physicochemical properties of this adhesive, as well as its anti-MMP potential [177]. DC and Knoop microhardness were not impaired. The adhesive showed dose-dependent antimicrobial and anti-MMP properties while preserving cell viability. Furthermore, Yan et al. [178] reported that CHX-encapsulated mesoporous silica-modified (1 and 5%) dentin adhesives can inhibit *Streptococcus mutans* while preserving DC and bond strength after collagenase aging of 1 month. In the group containing a higher concentration of the particles (10%), DC as well as bond strength were impaired. This was probably due to the tendency of nanoparticles to form clusters when they are present in a higher concentration, which was confirmed using FEISEM. The release of CHX was measured for 30 days and reached a plateau after day 10. Other mechanical properties of this adhesive should be investigated, as well as its anti-enzymatic potential. Furthermore, the ability of the nanocarriers of therapeutic agents to penetrate between the demineralized collagen fibrils should be considered and investigated due to their size and the small intermolecular spaces between collagen fibrils. In the case that nanoparticles could not infiltrate resin tags, therapeutic agents could not be delivered to the most critical parts of the hybrid layer.

Although all these approaches are valid, the most optimal way to singlehandedly reduce collagen degradation would be biomimetic remineralization, which would protect the collagen fibrils, cover and inactivate proteases, remove the remaining water, and enhance the mechanical properties of the hybrid layer. Recently, there have been reports that the use of primers doped with analogs of phosphoproteins and Ca/P-doped SE adhesives leads to biomimetic remineralization, with the preservation of bond strength and better mechanical properties of the hybrid layer [179,180]. Analogs of phosphoproteins play a very important role in the mineralization since, without them, the mineralization occurs only in the form of extrafibrillar mineral deposits [14,181–183]. Before transiting from this exciting *in vitro* to clinical concept, there is a long path to be crossed, but the future seems to carry innovative solutions, which could lead us to the next era in adhesive dentistry.

6. Pre-treatment agents of the dental substrate

Tooth whitening is a common esthetic procedure, which may be accompanied by some undesirable side effects. One of these potential drawbacks is the lower bond strength of resin-based restorative materials following the bleaching procedure [184,185]. The bond strength reduction has been associated with the residual oxygen derived from the hydrogen peroxide contained in the whitening agent that remains entrapped in the tooth surface, which can prevent the polymerization of the adhesive monomers [186]. A delayed placement of the restoration of at least 1 week following the bleaching procedure may improve the bond strength, allowing the elimination of residual oxygen. If the bonding procedure cannot be postponed, the use of antioxidant agents [187] or an increased polymerization time may partly compensate for the conversion inhibition [46,188].

Hydrogen peroxide can also be used as an endodontic irrigant, to help in removing residual pulp-tissue and debris produced by canal instrumentation. Similarly to tooth whitening, canal irrigation using hydrogen peroxide has been correlated to lower bond strength of resin adhesives and cements [189]. Hydrogen peroxide reacts with sodium hypochlorite, the most commonly used irrigant in endodontics, releasing water and oxygen, both of which are able to affect the polymerization of resin materials negatively.

In endodontics, RC-Prep (Premier Dental Products) is used as a lubricant and demineralizing agent and contains polyethylene glycol (Carbowax, Dow Chemical), which cannot be completely eliminated by canal irrigation and has also been found to inhibit resin polymerization, reducing the bond strength of resin adhesives and cements. It has been shown that the application of 10% ascorbic acid after RC-Prep use can neutralize the negative effect of polyethylene glycol and improve bond strength values [190].

Also, eugenol, a common component of some endodontic sealants and zinc oxide–eugenol temporary materials, can negatively affect bond strength values because it can infiltrate the dentin substrate [191]. Eugenol is a phenolic compound that can inhibit monomer polymerization, acting as a radical scavenger [192]. When eugenol-based materials are used prior to the application of resin compounds, the contaminated tooth substrate should be thoroughly cleaned both mechanically and by scrubbing the surface with a detergent or alcohol to remove the oily eugenol remnants, in order to prevent polymerization inhibition and bond strength reduction [193–195].

7. Intraradicular polymerization of adhesives

Following root canal treatment, non-vital teeth usually demonstrate an extensive loss of dental structure and the use of fiber posts and core systems to retain the final restoration [196] has been widely investigated and supported by clinical [197,198] and laboratory studies [197,199].

However, adhesion inside the root canal can be impaired by several factors [27,200]. Besides the influence of endodontic irrigants and cements already mentioned, the adverse geometric feature of the root canal [201], the peculiar characteristics of the post space [202] and possible incompatibilities between simplified adhesives and dual-cure resin-based cements [201] are important problems that affect polymerization quality and, consequently, the bond strength within the endodontic space. Some of these factors could not be limited and attenuated by the control of clinical steps and are strongly related to the root canal itself [203].

The cavity configuration factor (C-factor), defined as the ratio of the bonded to the unbonded surface area, of an endodontic post space has been estimated to be higher than 200, while coronal restoration values range between 1 and 5 [204]. During the polymerization procedure, the shrinkage stress relief of resin-based materials is possible due to the presence of large unbonded or freely shrinking, surfaces. However, when the unbonded surface area becomes small, there is insufficient stress relief via resin flow and a high probability to cause debonding of the luting material from the intra-radicular dentin [201]. Previous authors showed that the geometric factors of the cavity have an important influence on contraction stress, and post space depth has a greater influence than does diameter [205]. Thus, considering the configuration of the endodontic cavity, the development of large contraction stress during the curing procedure cannot be avoided, and can only be controlled through the rheological and viscoelastic properties of the luting materials [200].

Furthermore, the narrow diameter of the post space limits the passage of the curing light necessary for a correct polymerization, and the depth of the post space reduces the radiant energy in relation to the inverse square of the distance from the light source, thus affecting the degree of conversion of the material [206]. It has been demonstrated that a complete polymerization cannot be guaranteed when the material is placed deeper than 4–5 mm because of the limited transmission of light through intraradicularly placed adhesive [207,208]. Further, the bond strength of fiber posts has been shown to vary significantly based on the region of the root, with lower strengths in the apical portion of the post space compared to those in the coronal region [207].

For the above mentioned reasons an adhesive protocol using a light-cured resin system is not considered ideal due to the influence of reduced light radiant power produced by the shadowing of the tooth structure and the light scattering and attenuation within the resin cement and the post [209,210]. Therefore, both dual-cure adhesive systems and resin cements, such as materials combining self-curing and light-curing capabilities, have been suggested. Although the dual-curing systems allow use with limited light penetration, some authors reported that their activation is in any case primarily dependent on light presence [211,212]. Therefore, sufficient light penetration and energy through the root canal remains a fundamental requirement, even when dual-cure resin cements are used for post-fixation [213,214].

Many post systems available on the market are claimed to be 'translucent' and allow light to pass through the dowel leading to a higher initial polymerization of the resin cement [215]. However, even if translucent, fiber posts will limit light transmission to values lower than 40% of incident light and may not guarantee an adequate degree of conversion of the resin especially at the tip end [211]. In addition, several studies reported that the light transmitted through the post was drastically decreased when the depth from the top of the post was more than 4–6 mm [208,212,216], allowing insufficient transmission of light to polymerize the resin [208,212]. Furthermore, several manufacturers propose to light cure both the bonding agent and the dual cement through the translucent post. However, the resin cement layer could prevent adhesive polymerization because of light radiant power attenuation [217].

Some one-step self-etching adhesives are not compatible with chemically or dual-cured resin cements [218,219] due to the acidic resin monomers present in these systems [204,220]. The acidic monomers tend to react with the basic aromatic tertiary amines contained in the composite cement, inhibiting its polymerization [204]. Thus the use of one-step self-etching adhesives is discouraged in combination with these luting materials, even though a ternary catalyst might help overcome the acid-base reaction [204,220].

In contrast, three-step etch-and-rinse and two-step self-etching adhesives that do not include an acidic monomer in their bonding agent are compatible with chemically or dual-cured resin cements because of the presence of the hydrophobic adhesive layer, which works as an intermediate coat preventing the contact with the acidic monomers and the adverse acid-base reaction [218].

8. Curing lights

Choosing a curing device may not be as simple as it seems because not all light-curing units are comparable. There are variables in the light source type, in the light output and in the configuration of the curing tip [221]. Halogen devices were once the most widely used light-curing units for a long time. These units produce both UV and white light that must be filtered to minimize heat and ensure output of light primarily in the blue region of the spectrum [222]. Most of the total energy produced by a halogen light is converted to heat, which must be dispersed using a small fan incorporated in the device, and no more than 0.5% of the wavelength produced is useful for polymerization [222,223]. The more recent curing lights introduced on the market are the LED units, based on light-emitting diode technology, which have become rapidly popular due to their long service life, low weight and small dimensions, the absence of any filters and the use of battery power that eliminates the need for cumbersome electrical cords [222,223].

Each curing light emits its own spectral radiant power and the wavelength emitted should match the absorption peak of the photoinitiator used in the resin material [224,225]. The most common photoinitiator, camphoroquinone, has an absorption peak in the visible range (centered around 468–470 nm). Alternative photoinitiators such as PPD and TPO have lower absorbance peaks than CQ [223], being mostly absorbing in the UV region, but extending to the low wavelengths of the visible (near 400 nm). Curing lights with a wide spectral radiant power, such as the filtered light from halogen lights, cover the absorbance peaks of all photoinitiators. The narrow spectral radiant powers, such as that found in single peak LED units, are unable to cure materials containing PPD and TPO as their light output was typically restricted to above 420 nm. However, some LED units have addressed this issue by including both the main blue emitting LEDs as well as additional violet emitting LEDs with outputs near 400–410 nm. These "polywave"^{TM} units have greater potential to polymerize all of the photoinitiators currently being used [223,224].

The parameter that manufacturers generally use to describe a curing light is its tip irradiance (radiant exitance), expressed as power per unit area (mW/cm^2) according to the ISO 10650 standard (ISO 2018) [226]. Usually, a photocuring unit should have a minimum radiant exitance of 600–1000 mW/cm^2 [227]. In clinical practice, the irradiance can be checked using in-office dental radiometers. Although these devices may not be as accurate as using more sophisticated laboratory equipment [225], they typically are reproducible and provide important information about the light output over time [223]. Ideally the diameter of the detector needs to be equal to or smaller than the light tip [223], and the radiometer must be specifically calibrated for the light type being assessed (halogen or LED). It is important to continually monitor the curing unit, as light irradiance can be reduced due to chipping and fracture of the light tip or the presence of cured resin adhering to the light tip [228]. A recent survey performed in U.S. dental offices showed that light-curing units used in clinical practice had several problems, potentially affecting the curing performance, suggesting that practitioners should be more careful about the choice and the maintenance of curing lights [229]. Light output can also be reduced up to 40% when certain infection control covers are applied over the curing tip [230,231], so the irradiance of the curing device should be measured keeping the plastic barrier on to calculate the exact output during clinical service.

Even though commercial dental radiometers can measure the irradiance of the curing light, they do not provide any information about its spectral radiant power. More advanced and precise equipment is necessary to perform such measurements, such as calibrated spectrometer-based systems [225]. It is unlikely that dental offices are equipped with this kind of instrumentations, so it would be useful for all manufacturers to provide the spectral radiant power information along with the directions for use for their curing units [225]. Spectral radiant power expresses the homogeneity of the beam emitted by the curing device because the light is not uniformly distributed across the curing tip. Some lights have a light beam uniformly distributed over the entire light tip area, while in other lights the beam is concentrated mainly at the center of the tip or is unevenly distributed, with a spectral, or beam profile, characterized by peaks and valleys [232]. This is particularly true for many poly-wave LED curing lights that must use multiple LEDs, whose beam is not homogeneously irradiated due to the locations of the different LED chips, resulting in "hot" areas of high-intensity light energy and "cold" areas, where only a small amount of light is being emitted [224,232]. In clinical conditions, an inhomogeneous beam means that different parts of the resin material may receive variable irradiance levels, and potentially some areas may not be adequately polymerized [232]. This may be further complicated by the fact that many light guides for LED curing lights have a small tip diameter and do not completely cover the restoration area [233]. The advice is then to cure each portion of the material, overlapping surfaces to ensure complete photo-polymerization [223]. Changing the position of the tip is also recommended when the curing tip is big enough to cover the restoration, but the beam is not homogeneous [232].

9. Polymerization technique

Most dental research is conducted under ideal conditions with the curing light fixed directly above the specimen. This does not occur clinically and the actual distance between the tip and the material is very important, both clinically and in research because the irradiance received can be very different as the distance away from the light tip increases or the angle of the light tip to the specimen increases. For example when curing dental resins within cavity preparations due to the presence of cusps or matrix bands [228] or where the operator is not looking at what they are doing, the distance or angle of the light tip is not the same as in the laboratory [228]. In addition, using plastic barriers helps the operator to keep the curing tip as close to the tooth as possible without contaminating the tip, but they reduce the tip irradiance. Indeed, irradiance is strongly reduced as an inverse square relation to the distance from the tip [234,235]. The gingival margin of the proximal box of Class II restorations is particularly prone to bond failure due to suboptimal light curing [228]. When curing adhesives in deep Class II boxes, exposure time should be extended up to 40–60 s to guarantee an adequate degree of conversion [236–238], but at the same time taking care not to damage the pulp or soft tissues [239].

The distance of the tip is not the only thing that should be controlled during light curing. Maintaining the tip at a right angle, with the light tip parallel to the material surface, is also important because an incorrect inclination of the curing tip can significantly reduce the applied irradiance [228,240]. For some lights, the size or the angle of the tip can limit access to the restoration surface and thus the results obtained in the laboratory using that particular light must also be verified under simulated clinical conditions, where tooth position and the patient's mouth opening can interfere with the correct positioning of the light tip [228,240–242].

Wearing protective glasses to prevent acute and chronic retinal damage from exposure to the blue light from curing lights (the 'blue light hazard') has an additional major advantage: the operator can watch what they are doing and keep the light in the correct position [228].

In order to calculate the radiant exposure to obtain an adequate polymerization, some have tried to apply the exposure reciprocity law, where irradiance, described as milliWatt/area (mW/cm^2), is multiplied by the light exposure time to provide the energy/area delivered by the curing light [243,244]. This encouraged a tendency among manufacturers to suggest that using a curing light that emitted a high irradiance could reduce the exposure time. However, exposure reciprocity is incorrect from a theoretical standpoint, and delivering a low irradiance for a long exposure time does not give the same results as delivering a very high irradiance for a short time, and different combinations of time and irradiance can lead to significant differences in the material properties [243,244]. Unfortunately, most manufacturers suggest a single exposure duration regardless of the material type, shade, or clinical distance from the tip. Usually, manufacturers of resin materials recommend specific exposure times for their products that often do not match those of the light manufacturers. Moreover, these instructions are usually based on ideal laboratory conditions, using a new curing light, kept in direct contact (i.e., at 0 mm) with a material of known thickness [225]. Rather than simply stating a exposure time, manufacturers should indicate the radiant exposure required to properly cure their material [245]. Exposure time should be extended to compensate for the attenuation of light radiant power due to unfavorable clinical conditions. Additionally, some previous studies have reported that the exposure time recommended for dental adhesives are not adequate to obtain an optimal polymerization, even under ideal laboratory conditions [45,46], and longer exposure times are recommended. However, increasing the exposure may result in the generation of heat within the tooth and surrounding tissues. Even LEDs, which were initially claimed to be "cold" lights when they were first marketed, still produce heat up to 93% of their total energy [246]. The temperature increase is more pronounced during photopolymerization of the adhesive as compared with composites [247,248]. In case of a prolonged exposure, the tooth should be air-cooled during the photocuring procedure, or an interval of 1–2 s should be included after every 10 s of light exposure [232].

10. Conclusions

The stability of the adhesive layer is strongly influenced by the degree of conversion of the bonding system. Several factors may interfere with this reaction, and meticulous observance of the adhesive application and the polymerization protocol is necessary to guarantee optimal properties of the material. Further research is needed to clarify the role played by the output from the curing light and its osition in the photocuring reaction and by molecules that have been proposed as additives in adhesive formulations to counteract the degradation of the adhesive interface over time.

REFERENCES

[1] Buonocore MG. A simple method of increasing the adhesion of acrylic filling materials to enamel surfaces. J Dent Res 1955;34:849–53, http://dx.doi.org/10.1177/00220345550340060801.

[2] Truffier-Boutry D, Place E, Devaux J, Leloup G. Interfacial layer characterization in dental composite. J Oral Rehabil 2003;30:74–7, http://dx.doi.org/10.1046/j.1365-2842.2003.01008.x.

[3] Endo T, Osada T, Finger WJ, Hoffmann M, Kanehira M, Komatsu M. Effect of oxygen inhibition of self-etching adhesives on enamel–dentin polymer bond. J Adhes Dent 2007;9:33–8.

[4] Pashley DH, Tay FR, Breschi L, Tjäderhane L, Carvalho RM, Carrilho M, et al. State of the art etch-and-rinse adhesives. Dent Mater 2011;27:1–16, http://dx.doi.org/10.1016/j.dental.2010.10.016.

[5] Van Meerbeek B, Yoshihara K, Yoshida Y, Mine A, De Munck J, Van Landuyt KL. State of the art of self-etch adhesives. Dent Mater 2011;27:17–28, http://dx.doi.org/10.1016/j.dental.2010.10.023.

[6] Nakabayashi N, Nakamura M, Yasuda N. Hybrid layer as a dentin-bonding mechanism. J Esthet Dent 1991;3:133–8.

[7] Nakabayashi N. The hybrid layer: a resin-dentin composite. Proc Finn Dent Soc 1992;88(Suppl 1):321–9.

[8] Nakabayashi N, Kojima K, Masuhara E. The promotion of adhesion by the infiltration of monomers into tooth substrates. J Biomed Mater Res 1982;16:265–73.

[9] Van Meerbeek B, De Munck J, Yoshida Y. Adhesion to enamel and dentin: current status and future challenges. Oper Dent 2003;28:215–35.

[10] Asmussen E, Hansen E, Peutzfeldt A. Influence of the solubility parameter of intermediary resin on the effectiveness of the gluma bonding system. J Dent Res 1991;70:1290–3.

[11] Peumans M, Kanumilli P, De Munck J, Van Landuyt K, Lambrechts P, Van Meerbeek B. Clinical effectiveness of contemporary adhesives: a systematic review of current clinical trials. Dent Mater 2005;21:864–81, http://dx.doi.org/10.1016/j.dental.2005.02.003.

[12] Yoshida Y, Nagakane K, Fukuda R, Nakayama Y, Okazaki M, Shintani H, et al. Comparative study on adhesive performance of functional monomers. J Dent Res 2004;83:454–8, http://dx.doi.org/10.1177/154405910408300604.

[13] Van Landuyt K, Snauwaert J, De Munck J, Peumans M, Yoshida Y, Poitevin A, et al. Systematic review of the chemical composition of contemporary dental adhesives. Biomaterials 2007;28:3757–85.

[14] Breschi L, Maravic T, Cunha SR, Comba A, Cadenaro M, Tjäderhane L, et al. Dentin bonding systems: from dentin collagen structure to bond preservation and clinical applications. Dent Mater 2018;34:78–96, http://dx.doi.org/10.1016/j.dental.2017.11.005.

[15] Hilton TJ, Breschi L, Cadenaro M, Mazzoni M, Ferracane J. Adhesion to enamel and dentin. In: Hilton T, Ferracane J, Broome J, editors. Summitt's fundamental of operative dentistry: a contemporary approach. 4th ed. Hanover Park, IL: Quintessence Books; 2013.

[16] Swift EJ, Perdigão J, Heymann HO. Bonding to enamel and dentin: a brief history and state of the art, 1995. Quintessence Int 1995;26:95–110.

[17] Malacarne J, Carvalho RM, de Goes MF, Svizero N, Pashley DH, Tay FR, et al. Water sorption/solubility of dental adhesive resins. Dent Mater 2006;22:973–80, http://dx.doi.org/10.1016/j.dental.2005.11.020.

[18] Liu Y, Tjäderhane L, Breschi L, Mazzoni A, Li N, Mao J, et al. Limitations in bonding to dentin and experimental strategies to prevent bond degradation. J Dent Res 2011;90:953–68, http://dx.doi.org/10.1177/0022034510391799.

[19] Toledano M, Osorio R, de Leonardi G, Rosales-Leal JI, Ceballos L, Cabrerizo-Vilchez MA. Influence of self-etching primer on the resin adhesion to enamel and dentin. Am J Dent 2001;14:205–10.

[20] Hanabusa M, Mine A, Kuboki T, Momoi Y, Van Ende A, Van Meerbeek B, et al. Bonding effectiveness of a new 'multi-mode' adhesive to enamel and dentine. J Dent 2012;40:475–84, http://dx.doi.org/10.1016/j.jdent.2012.02.012.

[21] Barros J, Myaki S, Nor J, Peters M. Effect of bur type and conditioning on the surface and interface of dentine. J Oral Rehabil 2005;32:849–56, http://dx.doi.org/10.1111/j.1365-2842.2005.01507.x.

[22] Oliveira SS, Pugach MK, Hilton JF, Watanabe LG, Marshall SJ, Marshall GW. The influence of the dentin smear layer on adhesion: a self-etching primer vs. a total-etch system. Dent Mater 2003;19:758–67.

[23] Dias WR, Pereira PN, Swift EJ. Effect of bur type on microtensile bond strengths of self-etching systems to human dentin. J Adhes Dent 2004;6:195–203.

[24] Van Landuyt K, Kanumilli P, De Munck J, Peumans M, Lambrechts P, Van Meerbeek B. Bond strength of a mild self-etch adhesive with and without prior acid-etching. J Dent 2006;34:77–85, http://dx.doi.org/10.1016/j.jdent.2005.04.001.

[25] Cardoso M, De Almeida Neves A, Mine A, Coutinho E, Van Landuyt K, De Munck J, et al. Current aspects on bonding effectiveness and stability in adhesive dentistry. Aust Dent J 2011;56:31–44, http://dx.doi.org/10.1111/j.1834-7819.2011.01294.x.

[26] Frassetto A, Breschi L, Turco G, Marchesi G, Di Lenarda R, Tay FR, et al. Mechanisms of degradation of the hybrid layer in adhesive dentistry and therapeutic agents to improve bond durability — a literature review. Dent Mater 2016;32:e41–53, http://dx.doi.org/10.1016/j.dental.2015.11.007.

[27] Breschi L, Mazzoni A, Ruggeri A, Cadenaro M, Di Lenarda R, De Stefano Dorigo E. Dental adhesion review: aging and stability of the bonded interface. Dent Mater 2008;24:90–101, http://dx.doi.org/10.1016/j.dental.2007.02.009.

[28] Tjäderhane L. Dentin bonding: can we make it last? Oper Dent 2015;40:4–18, http://dx.doi.org/10.2341/14-095-BL.

[29] Van Nieuwenhuysen J-P, D'Hoore W, Carvalho J, Qvist V. Long-term evaluation of extensive restorations in permanent teeth. J Dent 2003;31:395–405.

[30] Rho Y-J, Namgung C, Jin B-H, Lim B-S, Cho B-H. Longevity of direct restorations in stress-bearing posterior cavities: a retrospective study. Oper Dent 2013;38:572–82, http://dx.doi.org/10.2341/12-432-C.

[31] Kopperud SE, Tveit AB, Gaarden T, Sandvik L, Espelid I. Longevity of posterior dental restorations and reasons for failure. Eur J Oral Sci 2012;120:539–48, http://dx.doi.org/10.1111/eos.12004.

[32] National Institute of Dental and Craniofacial Reearch (NIDCR). Nidcr NI of D and CR. Strategic plan 2009–2013. Bethseda, MD: National Institute of Dental and Craniofacial Reearch (NIDCR); 2009.

[33] Rasines Alcaraz MG, Veitz-Keenan A, Sahrmann P, Schmidlin PR, Davis D, Iheozor-Ejiofor Z. Direct composite resin fillings versus amalgam fillings for permanent or adult posterior teeth. Cochrane Database Syst Rev 2014;31, http://dx.doi.org/10.1002/14651858.CD005620.pub2. CD005620.

[34] Maravic T, Mazzoni A, Comba A, Scotti N, Checchi V, Breschi L. How stable is dentin as a substrate for bonding? Curr Oral Health Rep 2017;4:248–57, http://dx.doi.org/10.1007/s40496-017-0149-8.

[35] Mjör IA, Shen C, Eliasson ST, Richter S. Placement and replacement of restorations in general dental practice in Iceland. Oper Dent 2002;27:117–23.

[36] Hashimoto M. A review — micromorphological evidence of degradation in resin–dentin bonds and potential preventional solutions. J Biomed Mater Res B Appl Biomater 2010;92:268–80, http://dx.doi.org/10.1002/jbm.b.31535.

[37] De Munck J, Van Landuyt K, Peumans M, Poitevin A, Lambrechts P, Braem M, et al. A critical review of the durability of adhesion to tooth tissue: methods and results. J Dent Res 2005;84:118–32, http://dx.doi.org/10.1177/154405910508400204.

[38] Koshiro K, Inoue S, Tanaka T, Koase K, Fujita M, Hashimoto M, et al. In vivo degradation of resin–dentin bonds produced by a self-etch vs. a total-etch adhesive system. Eur J Oral Sci 2004;112:368–75, http://dx.doi.org/10.1111/j.1600-0722.2004.00141.x.

[39] Hashimoto M, Ohno H, Sano H, Kaga M, Oguchi H. In vitro degradation of resin–dentin bonds analyzed by microtensile bond test, scanning and transmission electron microscopy. Biomaterials 2003;24:3795–803, http://dx.doi.org/10.1016/S0142-9612(03)00262-X.

[40] Breschi L, Lopes M, Gobbi P, Mazzotti G, Falconi M, Perdigão J. Dentin proteoglycans: an immunocytochemical FEISEM study. J Biomed Mater Res 2002;61:40–6.

[41] Oyarzún A, Rathkamp H, Dreyer E. Immunohistochemical and ultrastructural evaluation of the effects of phosphoric acid etching on dentin proteoglycans. Eur J Oral Sci 2000;108:546–54.

[42] Lohbauer U, Rahiotis C, Krämer N, Petschelt A, Eliades G. The effect of different light-curing units on fatigue behavior and degree of conversion of a resin composite. Dent Mater 2005;21:608–15, http://dx.doi.org/10.1016/j.dental.2004.07.020.

[43] Ferracane JL, Mitchem JC, Condon JR, Todd R. Wear and marginal breakdown of composites with various degrees of cure. J Dent Res 1997;76:1508–16, http://dx.doi.org/10.1177/00220345970760081401.

[44] Vandewalle KS, Ferracane JL, Hilton TJ, Erickson RL, Sakaguchi RL. Effect of energy density on properties and marginal integrity of posterior resin composite restorations. Dent Mater 2004;20:96–106.

[45] Cadenaro M, Antoniolli F, Sauro S, Tay FR, Di Lenarda R, Prati C, et al. Degree of conversion and permeability of dental adhesives. Eur J Oral Sci 2005;113:525–30, http://dx.doi.org/10.1111/j.1600-0722.2005.00251.x.

[46] Breschi L, Cadenaro M, Antoniolli F, Sauro S, Biasotto M, Prati C, et al. Polymerization kinetics of dental adhesives cured with LED: correlation between extent of conversion and permeability. Dent Mater 2007;23:1066–72, http://dx.doi.org/10.1016/J.DENTAL.2006.06.040.

[47] Leprince JG, Palin WM, Hadis MA, Devaux J, Leloup G. Progress in dimethacrylate-based dental composite technology and curing efficiency. Dent Mater 2013;29:139–56, http://dx.doi.org/10.1016/J.DENTAL.2012.11.005.

[48] Ferracane JL. Hygroscopic and hydrolytic effects in dental polymer networks. Dent Mater 2006;22:211–22, http://dx.doi.org/10.1016/j.dental.2005.05.005.

[49] Spencer P, Ye Q, Park J, Topp EM, Misra A, Marangos O, et al. Adhesive/dentin interface: the weak link in the composite restoration. Ann Biomed Eng 2010;38:1989–2003, http://dx.doi.org/10.1007/s10439-010-9969-6.

[50] Tay FR, Frankenberger R, Krejci I, Bouillaguet S, Pashley DH, Carvalho RM, et al. Single-bottle adhesives behave as permeable membranes after polymerization. I. In vivo evidence. J Dent 2004;32:611–21, http://dx.doi.org/10.1016/J.JDENT.2004.04.006.

[51] Chersoni S, Suppa P, Grandini S, Goracci C, Monticelli F, Yiu C, et al. *In vivo* and *in vitro* permeability of one-step self-etch adhesives. J Dent Res 2004;83:459–64, http://dx.doi.org/10.1177/154405910408300605.

[52] Wang Y, Spencer P. Hybridization efficiency of the adhesive/dentin interface with wet bonding. J Dent Res 2003;82:141–5, http://dx.doi.org/10.1177/154405910308200213.

[53] Ito S, Hashimoto M, Wadgaonkar B, Svizero N, Carvalho RM, Yiu C, et al. Effects of resin hydrophilicity on water sorption and changes in modulus of elasticity. Biomaterials 2005;26:6449–59, http://dx.doi.org/10.1016/j.biomaterials.2005.04.052.

[54] Yoshida E, Uno S, Nodasaka Y, Kaga M, Hirano S. Relationship between water status in dentin and interfacial morphology in all-in-one adhesives. Dent Mater 2007;23:556–60, http://dx.doi.org/10.1016/j.dental.2006.03.014.

[55] Tay FR, Pashley DH. Have dentin adhesives become too hydrophilic? J Can Dent Assoc 2003;69:726–31, http://dx.doi.org/10.1016/S0109-5641(03)00110-6.

[56] Breschi L, Gobbi P, Lopes M, Prati C, Falconi M, Teti G, et al. Immunocytochemical analysis of dentin: a double-labeling technique. J Biomed Mater Res A 2003;67:11–7, http://dx.doi.org/10.1002/jbm.a.10048.

[57] Bedran-Russo AK, Pereira PN, Duarte WR, Okuyama K, Yamauchi M. Removal of dentin matrix proteoglycans by trypsin digestion and its effect on dentin bonding. J Biomed Mater Res B Appl Biomater 2008;85B:261–6, http://dx.doi.org/10.1002/jbm.b.30944.

[58] Armstrong SR, Vargas MA, Chung I, Pashley DH, Campbell JA, Laffoon JE, et al. Resin-dentin interfacial ultrastructure and microtensile dentin bond strength after five-year water storage. Oper Dent 2004;29.

[59] Pashley D, Tay F, Yiu C, Hashimoto M, Breschi L, Carvalho R. Collagen degradation by host-derived enzymes during aging. J Dent Res 2004;83:216–21.

[60] Van Meerbeek B, Van Landuyt K, De Munck J, Hashimoto M, Peumans M, Lambrechts P, et al. Technique-sensitivity of contemporary adhesives. Dent Mater J 2005;24:1–13.

[61] Pongprueksa P, Miletic V, Janssens H, Van Landuyt KL, De Munck J, Godderis L, et al. Degree of conversion and monomer elution of CQ/amine and TPO adhesives. Dent Mater 2014;30:695–701, http://dx.doi.org/10.1016/j.dental.2014.03.007.

[62] Van Landuyt KL, Krifka S, Hiller K-A, Bolay C, Waha C, Van Meerbeek B, et al. Evaluation of cell responses toward adhesives with different photoinitiating systems. Dent Mater 2015;31:916–27, http://dx.doi.org/10.1016/j.dental.2015.04.016.

[63] Tay FR, Pashley DH. Water treeing — a potential mechanism for degradation of dentin adhesives. Am J Dent 2003;16:6–12.

[64] Reis A, Ferreira SQ, Costa TR, Klein-Júnior CA, Meier MM, Loguercio AD. Effects of increased exposure times of simplified etch-and-rinse adhesives on the degradation of resin–dentin bonds and quality of the polymer network. Eur J Oral Sci 2010;118:502–9, http://dx.doi.org/10.1111/j.1600-0722.2010.00759.x.

[65] Navarra CO, Cadenaro M, Codan B, Mazzoni A, Sergo V, De Stefano Dorigo E, et al. Degree of conversion and interfacial nanoleakage expression of three one-step self-etch

adhesives. Eur J Oral Sci 2009;117:463–9, http://dx.doi.org/10.1111/j.1600-0722.2009.00654.x.
[66] Stansbury JW. Curing dental resins and composites by photopolymerization. J Esthet Dent 2000;12:300–8.
[67] Sperling LH. Introduction to physical polymer science. 4th ed. Hoboken, New Jersey: John Wiley & Sons, Inc.; 2006, http://dx.doi.org/10.1002/0471757128.
[68] Mazzoni A, Pashley DH, Tay FR, Gobbi P, Orsini G, Ruggeri A, et al. Immunohistochemical identification of MMP-2 and MMP-9 in human dentin: correlative FEI-SEM/TEM analysis. J Biomed Mater Res A 2009;88:697–703, http://dx.doi.org/10.1002/jbm.a.31920.
[69] Marchesi G, Navarra CO, Cadenaro M, Carrilho MR, Codan B, Sergo V, et al. The effect of ageing on the elastic modulus and degree of conversion of two multistep adhesive systems. Eur J Oral Sci 2010;118:304–10, http://dx.doi.org/10.1111/j.1600-0722.2010.00736.x.
[70] Saboia VP, Silva FC, Nato F, Mazzoni A, Cadenaro M, Mazzotti G, et al. Analysis of differential artificial ageing of the adhesive interface produced by a two-step etch-and-rinse adhesive. Eur J Oral Sci 2009;117:618–24, http://dx.doi.org/10.1111/j.1600-0722.2009.00665.x.
[71] Pongprueksa P, De Munck J, Inokoshi M, Van Meerbeek B. Polymerization efficiency affects interfacial fracture toughness of adhesives. Dent Mater 2018;34:684–92, http://dx.doi.org/10.1016/j.dental.2018.01.015.
[72] Zhang Y, Wang Y. The effect of hydroxyapatite presence on the degree of conversion and polymerization rate in a model self-etching adhesive. Dent Mater 2012;28:237–44, http://dx.doi.org/10.1016/j.dental.2011.10.003.
[73] Iwasa M, Tsubota K, Shimamura Y, Ando S, Miyazaki M, Platt JA. pH changes upon mixing of single-step self-etching adhesives with powdered dentin. J Adhes Dent 2011;13:207–12, http://dx.doi.org/10.3290/j.jad.a19240.
[74] Zhang Y, Wang Y. Improved degree of conversion of model self-etching adhesives through their interaction with dentine. J Dent 2012;40:57–63, http://dx.doi.org/10.1016/j.jdent.2011.10.004.
[75] Hanabusa M, Yoshihara K, Yoshida Y, Okihara T, Yamamoto T, Momoi Y, et al. Interference of functional monomers with polymerization efficiency of adhesives. Eur J Oral Sci 2016;124:204–9, http://dx.doi.org/10.1111/eos.12245.
[76] Wang Y, Spencer P. Continuing etching of an all-in-one adhesive in wet dentin tubules. J Dent Res 2005;84:350–4, http://dx.doi.org/10.1177/154405910508400411.
[77] Pashley DH, Tay FR. Aggressiveness of contemporary self-etching adhesives: Part II: etching effects on unground enamel. Dent Mater 2001;17:430–44.
[78] Tay FR, Pashley DH, Suh BI, Carvalho RM, Itthagarun A. Single-step adhesives are permeable membranes. J Dent 2002;30:371–82, http://dx.doi.org/10.1016/S0300-5712(02)00064-7.
[79] Spencer P, Wang Y. Adhesive phase separation at the dentin interface under wet bonding conditions. J Biomed Mater Res 2002;62:447–56, http://dx.doi.org/10.1002/jbm.10364.
[80] Wang Y, Spencer P, Hager C, Bohaty B. Comparison of interfacial characteristics of adhesive bonding to superficial versus deep dentine using SEM and staining techniques. J Dent 2006;34:26–34, http://dx.doi.org/10.1016/j.jdent.2005.03.004.
[81] Tay FR, Pashley DH, Yoshiyama M. Two modes of nanoleakage expression in single-step adhesives. J Dent Res 2002;81:472–6, http://dx.doi.org/10.1177/154405910208100708.
[82] Tay FR, King NM, Chan K, Pashley DH. How can nanoleakage occur in self-etching adhesive systems that demineralize and infiltrate simultaneously? J Adhes Dent 2002;4:255–69.
[83] Ye Q, Park J, Topp E, Spencer P. Effect of photoinitiators on the in vitro performance of a dentin adhesive exposed to simulated oral environment. Dent Mater 2009;25:452–8, http://dx.doi.org/10.1016/j.dental.2008.09.011.
[84] Cadenaro M, Breschi L, Rueggeberg FA, Suchko M, Grodin E, Agee K, et al. Effects of residual ethanol on the rate and degree of conversion of five experimental resins. Dent Mater 2009;25:621–8, http://dx.doi.org/10.1016/j.dental.2008.11.005.
[85] Park S-H, Roulet J-F, Heintze SD. Parameters influencing increase in pulp chamber temperature with light-curing devices: curing lights and pulpal flow rates. Oper Dent 2010;35:353–61, http://dx.doi.org/10.2341/09-234-L.
[86] Morães RR, Garcia JW, Wilson ND, Lewis SH, Barros MD, Yang B, et al. Improved dental adhesive formulations based on reactive nanogel additives. J Dent Res 2012;91:179–84, http://dx.doi.org/10.1177/0022034511426573.
[87] Dailing EA, Lewis SH, Barros MD, Stansbury JW. Construction of monomer-free, highly crosslinked, water-compatible polymers. J Dent Res 2014;93:1326–31, http://dx.doi.org/10.1177/0022034514552490.
[88] Gotti VB, Correr AB, Lewis SH, Feitosa VP, Correr-Sobrinho L, Stansbury JW. Influence of nanogel additive hydrophilicity on dental adhesive mechanical performance and dentin bonding. Dent Mater 2016;32:1406–13, http://dx.doi.org/10.1016/j.dental.2016.09.016.
[89] Cadenaro M, Antoniolli F, Codan B, Agee K, Tay FR, Dorigo EDS, et al. Influence of different initiators on the degree of conversion of experimental adhesive blends in relation to their hydrophilicity and solvent content. Dent Mater 2010;26:288–94, http://dx.doi.org/10.1016/j.dental.2009.11.078.
[90] Ye Q, Spencer P, Wang Y. Nanoscale patterning in crosslinked methacrylate copolymer networks: an atomic force microscopy study. J Appl Polym Sci Symp 2007;106:3843–51, http://dx.doi.org/10.1002/app.27044.
[91] Ye Q, Park JG, Topp E, Wang Y, Misra A, Spencer P. In vitro performance of nano-heterogeneous dentin adhesive. J Dent Res 2008;87:829–33, http://dx.doi.org/10.1177/154405910808700911.
[92] Wang Y, Spencer P, Yao X, Ye Q. Effect of coinitiator and water on the photoreactivity and photopolymerization of HEMA/camphoquinone-based reactant mixtures. J Biomed Mater Res A 2006;78:721–8, http://dx.doi.org/10.1002/jbm.a.30733.
[93] Tay FR, King NM, Suh BI, Pashley DH. Effect of delayed activation of light-cured resin composites on bonding of all-in-one adhesives. J Adhes Dent 2001;3:207–25.
[94] Ilie N, Hickel R. Can CQ be completely replaced by alternative initiators in dental adhesives? Dent Mater J 2008;27:221–8, http://dx.doi.org/10.4012/dmj.27.221.
[95] Moszner N, Salz U. Recent developments of new components for dental adhesives and composites. Macromol Mater Eng 2007;292:245–71, http://dx.doi.org/10.1002/mame.200600414.
[96] Salgado VE, Cavassoni D, Gonçalves APR, Pfeifer C, Moraes RR, Schneider LF. Photoinitiator system and water effects on CC conversion and solubility of experimental etch-and-rinse dental adhesives. Int J Adhes Adhes 2017;72:6–9, http://dx.doi.org/10.1016/j.ijadhadh.2016.09.001.
[97] Liu Y, Bai X, Liu YW, Wang Y. Light-cured self-etch adhesives undergo hydroxyapatite-triggered self-cure. J Dent Res 2016;95:334–41, http://dx.doi.org/10.1177/0022034515618959.
[98] Oliveira DC, Souza-Junior EJ, Dobson A, Correr AR, Brandt WC, Sinhoreti MA. Evaluation of phenyl-propanedione on yellowing and chemical-mechanical properties of

experimental dental resin-based materials. J Appl Oral Sci 2016;24:555–60, http://dx.doi.org/10.1590/1678-775720160058.

[99] Besse V, Derbanne MA, Pham T-N, Cook WD, Le Pluart L. Photopolymerization study and adhesive properties of self-etch adhesives containing bis(acyl)phosphine oxide initiator. Dent Mater 2016;32:561–9, http://dx.doi.org/10.1016/j.dental.2016.01.005.

[100] Borges BCD, de Sousa-Lima RX, Moreno GBP, Moreira DGL, Oliveira DCRS, Souza-Junior EJC, et al. Polymerization and adhesion behavior of experimental dental bonding materials with different initiator systems. J Adhes Sci Technol 2018;32:239–46, http://dx.doi.org/10.1080/01694243.2017.1352839.

[101] Oguri M, Yoshida Y, Yoshihara K, Miyauchi T, Nakamura Y, Shimoda S, et al. Effects of functional monomers and photo-initiators on the degree of conversion of a dental adhesive. Acta Biomater 2012;8:1928–34, http://dx.doi.org/10.1016/j.actbio.2012.01.013.

[102] Toba Y, Yasuike M, Usui Y. The ′onium butyltriphenylborates as novel donor–acceptor initiators for free radical photopolymerization. Chem Commun 1997;0:675–6, http://dx.doi.org/10.1039/a700579b.

[103] Toba Y, Usui Y, Konishi T, Ito O, Uesugi T. Visible light polymerization of acrylate using dialkylphenacylsulfonium butyltriphenylborate initiators: effect of the reduction potential of the sulfonium cation on the polymerization. Macromolecules 1999;32:6545–51, http://dx.doi.org/10.1021/ma990070u.

[104] Sato T, Kashino E, Fukumura N, Otsu T. Vinyl polymerization initiated by the binary system of tetraphenylborate salts and organic acids. Die Makromol Chemie 1972;162:9–18, http://dx.doi.org/10.1002/macp.1972.021620102.

[105] Jacobsen T, Finger WJ, Kanehira M. Air-drying time of self-etching adhesives vs. bonding efficacy. J Adhes Dent 2006;8:387–92.

[106] Pashley DH, Tay FR, Carvalho RM, Rueggeberg FA, Agee KA, Carrilho M, et al. From dry bonding to water-wet bonding to ethanol-wet bonding. A review of the interactions between dentin matrix and solvated resins using a macromodel of the hybrid layer. Am J Dent 2007;20:7–20.

[107] Holmes RG, Rueggeberg FA, Callan RS, Caughman F, Chan DCN, Pashley DH, et al. Effect of solvent type and content on monomer conversion of a model resin system as a thin film. Dent Mater 2007;23:1506–12, http://dx.doi.org/10.1016/j.dental.2007.01.007.

[108] Ye Q, Spencer P, Wang Y, Misra A. Relationship of solvent to the photopolymerization process, properties, and structure in model dentin adhesives. J Biomed Mater Res A 2007;80A:342–50, http://dx.doi.org/10.1002/jbm.a.30890.

[109] Paul SJ, Leach M, Rueggeberg FA, Pashley DH. Effect of water content on the physical properties of model dentine primer and bonding resins. J Dent 1999;27:209–14, http://dx.doi.org/10.1016/S0300-5712(98)00042-6.

[110] Hosaka K, Tagami J, Nishitani Y, Yoshiyama M, Carrilho M, Tay FR, et al. Effect of wet vs. dry testing on the mechanical properties of hydrophilic self-etching primer polymers. Eur J Oral Sci 2007;115:239–45, http://dx.doi.org/10.1111/j.1600-0722.2007.00452.x.

[111] Ikeda T, De Munck J, Shirai K, Hikita K, Inoue S, Sano H, et al. Effect of evaporation of primer components on ultimate tensile strengths of primer–adhesive mixture. Dent Mater 2005;21:1051–8, http://dx.doi.org/10.1016/j.dental.2005.03.010.

[112] Ikeda T, De Munck J, Shirai K, Hikita K, Inoue S, Sano H, et al. Effect of air-drying and solvent evaporation on the strength of HEMA-rich versus HEMA-free one-step adhesives. Dent Mater 2008;24:1316–23, http://dx.doi.org/10.1016/j.dental.2008.02.009.

[113] Pashley EL, Zhang Y, Lockwood EP, Rueggeberg FA, Pashley DH. Effects of HEMA on water evaporation from water–HEMA mixtures. Dent Mater 1998;14:6–10, http://dx.doi.org/10.1016/S0109-5641(98)00003-7.

[114] Hilton T, Schwartz R, Ferracane J. Fifth-generation bonding agent application technique effects on bond strength [abstract 214]. J Dent Res 1998;77:132, http://dx.doi.org/10.1177/0022034598077S101.

[115] Reis A, Klein-Junior CA, de Souza FH, Stanislawczuk R, Loguercio AD. The use of warm air stream for solvent evaporation: effects on the durability of resin–dentin bonds. Oper Dent 2010;35:29–36, http://dx.doi.org/10.2341/08-065-L.

[116] Cadenaro M, Breschi L, Antoniolli F, Navarra CO, Mazzoni A, Tay FR, et al. Degree of conversion of resin blends in relation to ethanol content and hydrophilicity. Dent Mater 2008;24:1194–200, http://dx.doi.org/10.1016/j.dental.2008.01.012.

[117] Malacarne-Zanon J, Pashley DH, Agee KA, Foulger S, Alves MC, Breschi L, et al. Effects of ethanol addition on the water sorption/solubility and percent conversion of comonomers in model dental adhesives. Dent Mater 2009;25:1275–84, http://dx.doi.org/10.1016/j.dental.2009.03.015.

[118] Wang Y, Spencer P. Quantifying adhesive penetration in adhesive/dentin interface using confocal Raman microspectroscopy. J Biomed Mater Res 2002;59:46–55, http://dx.doi.org/10.1002/jbm.1215.

[119] Frankenberger R, Pashley DH, Reich SM, Lohbauer U, Petschelt A, Tay FR. Characterisation of resin-dentine interfaces by compressive cyclic loading. Biomaterials 2005;26:2043–52, http://dx.doi.org/10.1016/j.biomaterials.2004.07.003.

[120] Sano H, Takatsu T, Ciucchi B, Honer J, Matthews W, Pashley D. Nanoleakage: leakage within the hybrid layer. Oper Dent 1995;20:18–25.

[121] Hannas AR, Pereira JC, Granjeiro JM, Tjäderhane L, Hannas AR, Pereira JC, et al. The role of matrix metalloproteinases in the oral environment. Acta Odontol Scand 2007;65:1–13, http://dx.doi.org/10.1080/00016350600963640.

[122] Vidal CM, Tjäderhane L, Scaffa PM, Tersariol IL, Pashley D, Nader HB, et al. Abundance of MMPs and cysteine cathepsins in caries-affected dentin. J Dent Res 2014;93:269–74, http://dx.doi.org/10.1177/0022034513516979.

[123] Nascimento FD, Minciotti CL, Geraldeli S, Carrilho MR, Pashley DH, Tay FR, et al. Cysteine cathepsins in human carious dentin. J Dent Res 2011;90:506–11, http://dx.doi.org/10.1177/0022034510391906.

[124] Visse R, Nagase H. Matrix metalloproteinases and tissue inhibitors of metalloproteinases: Structure, function, and biochemistry. Circ Res 2003;92:827–39, http://dx.doi.org/10.1161/01.RES.0000070112.80711.3D.

[125] Perumal S, Antipova O, Orgel JPRO. Collagen fibril architecture, domain organization, and triple-helical conformation govern its proteolysis. Proc Natl Acad Sci U S A 2008;105:2824–9, http://dx.doi.org/10.1073/pnas.0710588105.

[126] Mirigian LS, Makareeva E, Koistinen H, Itkonen O, Sorsa T, Stenman UH, et al. Collagen degradation by tumor-associated trypsins. Arch Biochem Biophys 2013;535:111–4, http://dx.doi.org/10.1016/j.abb.2013.03.008.

[127] Tjäderhane L, Nascimento FD, Breschi L, Mazzoni A, Tersariol IL, Geraldeli S, et al. Strategies to prevent hydrolytic degradation of the hybrid layer—a review. Dent Mater 2013;29:999–1011, http://dx.doi.org/10.1016/j.dental.2013.07.016.

[128] Hebling J, Pashley DH, Tjäderhane L, Tay FR. Chlorhexidine arrests subclinical degradation of dentin hybrid layers in vivo. J Dent Res 2005;84:741–6, http://dx.doi.org/10.1177/154405910508400811.

[129] Breschi L, Martin P, Mazzoni A, Nato F, Carrilho M, Tjäderhane L, et al. Use of a specific MMP-inhibitor (galardin) for preservation of hybrid layer. Dent Mater 2010;26:571–8, http://dx.doi.org/10.1016/j.dental.2010.02.007.

[130] Carrilho MR, Geraldeli S, Tay FR, de Goes M, Carvalho RM, Tjäderhane L, et al. In vivo preservation of the hybrid layer by chlorhexidine. J Dent Res 2007;86:529–33, http://dx.doi.org/10.1177/154405910708600608.

[131] Carrilho MR, Carvalho RM, de Goes MF, di Hipólito V, Geraldeli S, Tay FR, et al. Chlorhexidine preserves dentin bond in vitro. J Dent Res 2007;86:90–4, http://dx.doi.org/10.1177/154405910708600115.

[132] Seseogullari-Dirihan R, Mutluay MM, Vallittu P, Pashley DH, Tezvergil-Mutluay A. Effect of pretreatment with collagen crosslinkers on dentin protease activity. Dent Mater 2015;31:941–7, http://dx.doi.org/10.1016/j.dental.2015.05.002.

[133] Mazzoni A, Angeloni V, Sartori N, Duarte S, Maravic T, Tjäderhane L, et al. Substantivity of carbodiimide inhibition on dentinal enzyme activity over time. J Dent Res 2017;96:902–8, http://dx.doi.org/10.1177/0022034517708312.

[134] Bedran-Russo AK, Pereira PN, Duarte WR, Drummond JL, Yamauchi M. Application of crosslinkers to dentin collagen enhances the ultimate tensile strength. J Biomed Mater Res B Appl Biomater 2007;80:268–72, http://dx.doi.org/10.1002/jbm.b.30593.

[135] Breschi L, Mazzoni A, Nato F, Carrilho M, Visintini E, Tjäderhane L, et al. Chlorhexidine stabilizes the adhesive interface: a 2-year in vitro study. Dent Mater 2010;26:320–5, http://dx.doi.org/10.1016/j.dental.2009.11.153.

[136] Campos EA, Correr GM, Leonardi DP, Barato-Filho F, Gonzaga CC, Zielak JC. Chlorhexidine diminishes the loss of bond strength over time under simulated pulpal pressure and thermo-mechanical stressing. J Dent 2009;37:108–14, http://dx.doi.org/10.1016/j.jdent.2008.10.003.

[137] Loguercio AD, Hass V, Gutierrez MF, Luque-Martinez IV, Szesz A, Stanislawczuk R, et al. Five-year effects of chlorhexidine on the in vitro durability of resin/dentin interfaces. J Adhes Dent 2016;18:35–43, http://dx.doi.org/10.3290/j.jad.a35514.

[138] Zheng P, Zaruba M, Attin T, Wiegand A. Effect of different matrix metalloproteinase inhibitors on microtensile bond strength of an etch-and-rinse and a self-etching adhesive to dentin. Oper Dent 2014;40:80–6, http://dx.doi.org/10.2341/13-162-L.

[139] Brackett MG, Tay FR, Brackett WW, Dib A, Dipp FA, Mai S, et al. In vivo chlorhexidine stabilization of hybrid layers of an acetone-based dentin adhesive. Oper Dent 2009;34:379–83, http://dx.doi.org/10.2341/08-103.

[140] Mobarak EH. Effect of chlorhexidine pretreatment on bond strength durability of caries-affected dentin over 2-year aging in artificial saliva and under simulated intrapulpal pressure. Oper Dent 2011;36:649–60, http://dx.doi.org/10.2341/11-018-L.

[141] Leitune VC, Portella FF, Bohn PV, Collares FM, Samuel SMW. Influence of chlorhexidine application on longitudinal adhesive bond strength in deciduous teeth. Braz Oral Res 2011;25:388–92, http://dx.doi.org/10.1590/S1806-83242011000500003.

[142] Carrilho MR, Carvalho RM, Sousa EN, Nicolau J, Breschi L, Mazzoni A, et al. Substantivity of chlorhexidine to human dentin. Dent Mater 2010;26:779–85, http://dx.doi.org/10.1016/j.dental.2010.04.002.

[143] Kim J, Uchiyama T, Carrilho M, Agee KA, Mazzoni A, Breschi L, et al. Chlorhexidine binding to mineralized versus demineralized dentin powder. Dent Mater 2010;26:771–8, http://dx.doi.org/10.1016/j.dental.2010.04.001.

[144] Gendron R, Grenier D, Sorsa T, Mayrand D. Inhibition of the activities of matrix metalloproteinases 2, 8, and 9 by chlorhexidine. Clin Diagn Lab Immunol 1999;6:437–9.

[145] Tezvergil-Mutluay A, Mutluay MM, Gu LS, Zhang K, Agee KA, Carvalho RM, et al. The anti-MMP activity of benzalkonium chloride. J Dent 2011;39:57–64, http://dx.doi.org/10.1016/j.jdent.2010.10.003.

[146] Sabatini C, Ortiz PA, Pashley DH. Preservation of resin-dentin interfaces treated with benzalkonium chloride adhesive blends. Eur J Oral Sci 2015;123:108–15, http://dx.doi.org/10.1111/eos.12176.

[147] Hoshika T, Nishitani Y, Yoshiyama M, Key WO, Brantley W, Agee KA, et al. Effects of quaternary ammonium-methacrylates on the mechanical properties of unfilled resins. Dent Mater 2014;30:1213–23, http://dx.doi.org/10.1016/j.dental.2014.08.365.

[148] Imazato S, Tay FR, Kaneshiro AV, Takahashi Y, Ebisu S. An in vivo evaluation of bonding ability of comprehensive antibacterial adhesive system incorporating MDPB. Dent Mater 2007;23:170–6, http://dx.doi.org/10.1016/j.dental.2006.01.005.

[149] Imazato S, Kinomoto Y, Tarumi H, Ebisu S, Tay RF. Antibacterial activity and bonding characteristics of an adhesive resin containing antibacterial monomer MDPB. Dent Mater 2003;19:313–9, http://dx.doi.org/10.1016/S0109-5641(02)00060-X.

[150] Pashley D, Tay F, Imazato S. How to increase the durability of resin–dentin bonds. Compend Contin Educ Dent 2011;32:60–4.

[151] Tezvergil-Mutluay A, Agee KA, Mazzoni A, Carvalho RM, Carrilho M, Tersariol IL, et al. Can quaternary ammonium methacrylates inhibit matrix MMPs and cathepsins? Dent Mater 2015;31:e25–32, http://dx.doi.org/10.1016/j.dental.2014.10.006.

[152] Sulkala M, Wahlgren J, Larmas M, Sorsa T, Teronen O, Salo T, et al. The effects of MMP inhibitors on human salivary MMP activity and caries progression in rats. J Dent Res 2001;80:1545–9, http://dx.doi.org/10.1177/00220345010800061301.

[153] Lauhio A, Salo T, Tjäderhane L, Lähdevirta J, Golub LM, Sorsa T. Tetracyclines in treatment of rheumatoid arthritis. Lancet (London, England) 1995;346:645–6.

[154] Sorsa T, Tjäderhane L, Konttinen YT, Lauhio A, Salo T, Lee H, et al. Matrix metalloproteinases: contribution to pathogenesis, diagnosis and treatment of periodontal inflammation. Ann Med 2006;38:306–21, http://dx.doi.org/10.1080/07853890600800103.

[155] Bedran-Russo AK, Pashley DH, Agee K, Drummond JL, Miescke KJ. Changes in stiffness of demineralized dentin following application of collagen crosslinkers. J Biomed Mater Res B Appl Biomater 2008;86:330–4, http://dx.doi.org/10.1002/jbm.b.31022.

[156] Xu C, Wang Y. Cross-linked demineralized dentin maintains its mechanical stability when challenged by bacterial collagenase. J Biomed Mater Res B Appl Biomater 2011;96 B:242–8, http://dx.doi.org/10.1002/jbm.b.31759.

[157] Bedran-Russo AK, Pauli GF, Chen SN, McAlpine J, Castellan CS, Phansalkar RS, et al. Dentin biomodification: strategies, renewable resources and clinical applications. Dent Mater 2014;30:62–76, http://dx.doi.org/10.1016/j.dental.2013.10.012.

[158] Maravic T, Breschi L, Comba A, Cunha SR, Angeloni V, Nucci C, et al. Experimental use of an acrolein-based primer as

collagen cross-linker for dentine bonding. J Dent 2017;68:85–90, http://dx.doi.org/10.1016/j.jdent.2017.11.006.
[159] Seseogullari-Dirihan R, Apollonio F, Mazzoni A, Tjaderhane L, Pashley D, Breschi L, et al. Use of crosslinkers to inactivate dentin MMPs. Dent Mater 2016;32:423–32, http://dx.doi.org/10.1016/j.dental.2015.12.012.
[160] Mazzoni A, Angeloni V, Apolonio FM, Scotti N, Tjäderhane L, Tezvergil-Mutluay A, et al. Effect of carbodiimide (EDC) on the bond stability of etch-and-rinse adhesive systems. Dent Mater 2013;29:1040–7, http://dx.doi.org/10.1016/j.dental.2013.07.010.
[161] Tezvergil-Mutluay A, Mutluay MM, Agee KA, Seseogullari-Dirihan R, Hoshika T, Cadenaro M, et al. Carbodiimide cross-linking inactivates soluble and matrix-bound MMPs, in vitro. J Dent Res 2012;91:192–6, http://dx.doi.org/10.1177/0022034511427705.
[162] Mazzoni A, Apolonio FM, Saboia VPA, Santi S, Angeloni V, Checchi V, et al. Carbodiimide inactivation of MMPs and effect on dentin bonding. J Dent Res 2014;93:263–8, http://dx.doi.org/10.1177/0022034513516465.
[163] Bedran-Russo AK, Vidal CM, Dos Santos PH, Castellan CS. Long-term effect of carbodiimide on dentin matrix and resin–dentin bonds. J Biomed Mater Res B Appl Biomater 2010;94:250–5, http://dx.doi.org/10.1002/jbm.b.31649.
[164] Epasinghe DJ, Yiu CKY, Burrow MF. Effect of proanthocyanidin incorporation into dental adhesive on durability of resin–dentin bond. Int J Adhes Adhes 2015;63:145–51, http://dx.doi.org/10.1016/j.ijadhadh.2015.09.006.
[165] Liu Y, Dusevich V, Wang Y. Proanthocyanidins rapidly stabilize the demineralized dentin layer. J Dent Res 2013;92:746–52, http://dx.doi.org/10.1177/0022034513492769.
[166] Sadek FT, Braga RR, Muench A, Liu Y, Pashley DH, Tay FR. Ethanol wet-bonding challenges current anti-degradation strategy. J Dent Res 2010;89:1499–504, http://dx.doi.org/10.1177/0022034510385240.
[167] Ricci HA, Sanabe ME, de Souza Costa CA, Pashley DH, Hebling J. Chlorhexidine increases the longevity of in vivo resin–dentin bonds. Eur J Oral Sci 2010;118:411–6, http://dx.doi.org/10.1111/j.1600-0722.2010.00754.x.
[168] Moharam LM, Salem HN, Elgamily HM. The effect of incorporating different concentrations of chlorhexidine digluconate on the degree of conversion of an experimental adhesive resin. J Clin Exp Dent 2018;10 e:e371–7, http://dx.doi.org/10.4317/jced.54391.
[169] Cadenaro M, Pashley DH, Marchesi G, Carrilho M, Antoniolli F, Mazzoni A, et al. Influence of chlorhexidine on the degree of conversion and E-modulus of experimental adhesive blends. Dent Mater 2009;25:1269–74, http://dx.doi.org/10.1016/j.dental.2009.05.008.
[170] Stanislawczuk R, Pereira F, Muñoz MA, Luque I, Farago PV, Reis A, et al. Effects of chlorhexidine-containing adhesives on the durability of resin-dentine interfaces. J Dent 2014;42:39–47, http://dx.doi.org/10.1016/j.jdent.2013.11.002.
[171] da Silva EM, de Sá Rodrigues CU, de Oliveira Matos MP, de Carvalho TR, dos Santos GB, Amaral CM. Experimental etch-and-rinse adhesive systems containing MMP-inhibitors: physicochemical characterization and resin–dentin bonding stability. J Dent 2015;43:1491–7, http://dx.doi.org/10.1016/j.jdent.2015.10.004.
[172] Gotti VB, Feitosa VP, Sauro S, Correr-Sobrinho L, Leal FB, Stansbury JW, et al. Effect of antioxidants on the dentin interface bond stability of adhesives exposed to hydrolytic degradation. J Adhes Dent 2015;17:35–44, http://dx.doi.org/10.3290/j.jad.a33515.
[173] Yang H, Li K, Yan H, Liu S, Wang Y, Huang C. High-performance therapeutic quercetin-doped adhesive for adhesive-dentin interfaces. Sci Rep 2017;7:1–11, http://dx.doi.org/10.1038/s41598-017-08633-3.
[174] Pallan S, Furtado Araujo MV, Cilli R, Prakki A. Mechanical properties and characteristics of developmental copolymers incorporating catechin or chlorhexidine. Dent Mater 2012;28:687–94, http://dx.doi.org/10.1016/j.dental.2012.03.003.
[175] Bottino MC, Batarseh G, Palasuk J, Alkatheeri MS, Windsor LJ, Platt JA. Nanotube-modified dentin adhesive — physicochemical and dentin bonding characterizations. Dent Mater 2013;29:1158–65, http://dx.doi.org/10.1016/j.dental.2013.08.211.
[176] Feitosa SA, Palasuk J, Kamocki K, Geraldeli S, Gregory RL, Platt JA, et al. Doxycycline-encapsulated nanotube-modified dentin adhesives. J Dent Res 2014;93:1270–6, http://dx.doi.org/10.1177/0022034514549997.
[177] Palasuk J, Windsor LJ, Platt JA, Lvov Y, Geraldeli S, Bottino MC. Doxycycline-loaded nanotube-modified adhesives inhibit MMP in a dose-dependent fashion. Clin Oral Investig 2018;22:1243–52, http://dx.doi.org/10.1007/s00784-017-2215-y.
[178] Yan H, Wang S, Han L, Peng W, Yi L, Guo R, et al. Chlorhexidine-encapsulated mesoporous silica-modified dentin adhesive. J Dent 2018;78:83–90, http://dx.doi.org/10.1016/j.jdent.2018.08.012.
[179] Sauro S, Osorio R, Watson TF, Toledano M. Influence of phosphoproteins' biomimetic analogs on remineralization of mineral-depleted resin-dentin interfaces created with ion-releasing resin-based systems. Dent Mater 2015;31:759–77, http://dx.doi.org/10.1016/j.dental.2015.03.013.
[180] Abuna G, Feitosa VP, Correr AB, Cama G, Giannini M, Sinhoreti MA, et al. Bonding performance of experimental bioactive/biomimetic self-etch adhesives doped with calcium-phosphate fillers and biomimetic analogs of phosphoproteins. J Dent 2016;52:79–86, http://dx.doi.org/10.1016/j.jdent.2016.07.016.
[181] Gu L, Kim YK, Liu Y, Ryou H, Wimmer CE, Dai L, et al. Biomimetic analogs for collagen biomineralization. J Dent Res 2011;90:82–7, http://dx.doi.org/10.1177/0022034510385241.
[182] Kim J, Arola DD, Gu L, Kim YK, Mai S, Liu Y, et al. Functional biomimetic analogs help remineralize apatite-depleted demineralized resin-infiltrated dentin via a bottom–up approach. Acta Biomater 2010;6:2740–50, http://dx.doi.org/10.1016/j.actbio.2009.12.052.
[183] Kim YK, Gu L, Bryan TE, Kim JR, Chen L, Liu Y, et al. Mineralisation of reconstituted collagen using polyvinylphosphonic acid/polyacrylic acid templating matrix protein analogues in the presence of calcium, phosphate and hydroxyl ions. Biomaterials 2010;31:6618–27, http://dx.doi.org/10.1016/j.biomaterials.2010.04.060.
[184] Attin T, Hannig C, Wiegand A, Attin R. Effect of bleaching on restorative materials and restorations — a systematic review. Dent Mater 2004;20:852–61, http://dx.doi.org/10.1016/j.dental.2004.04.002.
[185] Lyons K, Ng B. Nightguard vital bleaching: a review and clinical study. N Z Dent J 1998;94:100–3.
[186] Arcari GM, Araújo E, Baratieri LN, Lopes GC. Microtensile bond strength of a nanofilled composite resin to human dentin after nonvital tooth bleaching. J Adhes Dent 2007;9:333–40.
[187] Feiz A, Mosleh H, Nazeri R. Evaluating the effect of antioxidant agents on shear bond strength of tooth-colored restorative materials after bleaching: a systematic review. J

Mech Behav Biomed Mater 2017;71:156–64, http://dx.doi.org/10.1016/j.jmbbm.2017.03.010.
[188] Cadenaro M, Breschi L, Antoniolli F, Mazzoni A, Di Lenarda R. Influence of whitening on the degree of conversion of dental adhesives on dentin. Eur J Oral Sci 2006;114:257–62, http://dx.doi.org/10.1111/j.1600-0722.2006.00351.x.
[189] Ari H, Erdemir A, Belli S. Evaluation of the effect of endodontic irrigation solutions on the microhardness and the roughness of root canal dentin. J Endod 2004;30:792–5.
[190] Morris M, Lee K, Agee K, Bouillaguet S, Pashley D. Effects of sodium hypochlorite and RC-prep on bond strengths of resin cement to endodontic surfaces. J Endod 2001;27:753–7, http://dx.doi.org/10.1097/00004770-200112000-00010.
[191] Kielbassa AM, Attin T, Hellwig E. Diffusion behavior of eugenol from zinc oxide-eugenol mixtures through human and bovine dentin in vitro. Oper Dent 1997;22:15–20.
[192] Carvalho CN, de Oliveira Bauer JR, Loguercio AD, Reis A. Effect of ZOE temporary restoration on resin–dentin bond strength using different adhesive strategies. J Esthet Restor Dent 2007;19:144–52, http://dx.doi.org/10.1111/j.1708-8240.2007.00087.x.
[193] Serafino C, Gallina G, Cumbo E, Ferrari M. Surface debris of canal walls after post space preparation in endodontically treated teeth: a scanning electron microscopic study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;97:381–7, http://dx.doi.org/10.1016/S1079210403006061.
[194] Serafino C, Gallina G, Cumbo E, Monticelli F, Goracci C, Ferrari M. Ultrasound effects after post space preparation: an SEM study. J Endod 2006;32:549–52, http://dx.doi.org/10.1016/J.JOEN.2005.07.003.
[195] Coniglio I, Magni E, Goracci C, Radovic I, Carvalho CA, Grandini S, et al. Post space cleaning using a new nickel titanium endodontic drill combined with different cleaning regimens. J Endod 2008;34:83–6, http://dx.doi.org/10.1016/j.joen.2007.10.019.
[196] Zicari F, Coutinho E, Scotti R, Van Meerbeek B, Naert I. Mechanical properties and micro-morphology of fiber posts. Dent Mater 2013;29:e45–52, http://dx.doi.org/10.1016/j.dental.2012.11.001.
[197] Bitter K, Kielbassa AM. Post-endodontic restorations with adhesively luted fiber-reinforced composite post systems: a review. Am J Dent 2007;20:353–60.
[198] Cagidiaco MC, Goracci C, Garcia-Godoy F, Ferrari M. Clinical studies of fiber posts: a literature review. Int J Prosthodont 2008;21:328–36.
[199] Goracci C, Grandini S, Bossù M, Bertelli E, Ferrari M. Laboratory assessment of the retentive potential of adhesive posts: a review. J Dent 2007;35:827–35, http://dx.doi.org/10.1016/J.JDENT.2007.07.009.
[200] Ferrari M, Carvalho CA, Goracci C, Antoniolli F, Mazzoni A, Mazzotti G, et al. Influence of luting material filler content on post cementation. J Dent Res 2009;88:951–6, http://dx.doi.org/10.1177/0022034509342851.
[201] Tay FR, Loushine RJ, Lambrechts P, Weller RN, Pashley DH. Geometric factors affecting dentin bonding in root canals: a theoretical modeling approach. J Endod 2005;31:584–9.
[202] Ferrari M, Mannocci F, Vichi A, Cagidiaco MC, Mjör IA. Bonding to root canal: structural characteristics of the substrate. Am J Dent 2000;13:255–60.
[203] Feilzer AJ, Dauvillier BS. Effect of TEGDMA/BisGMA ratio on stress development and viscoelastic properties of experimental two-paste composites. J Dent Res 2003;82:824–8, http://dx.doi.org/10.1177/154405910308201012.
[204] Bouillaguet S, Troesch S, Wataha JC, Krejci I, Meyer JM, Pashley DH. Microtensile bond strength between adhesive cements and root canal dentin. Dent Mater 2003;19:199–205.
[205] Braga RR, Ferracane JL. Alternatives in polymerization contraction stress management. Crit Rev Oral Biol Med 2004;15:176–84.
[206] Aravamudhan K, Rakowski D, Fan PL. Variation of depth of cure and intensity with distance using LED curing lights. Dent Mater 2006;22:988–94, http://dx.doi.org/10.1016/j.dental.2005.11.031.
[207] Lui JL. Depth of composite polymerization within simulated root canals using light-transmitting posts. Oper Dent 1994;19:165–8.
[208] Yoldas O, Alaçam T. Microhardness of composites in simulated root canals cured with light transmitting posts and glass-fiber reinforced composite posts. J Endod 2005;31:104–6.
[209] Musanje L, Darvell B. Curing-light attenuation in filled-resin restorative materials. Dent Mater 2006;22:804–17, http://dx.doi.org/10.1016/j.dental.2005.11.009.
[210] Faria-e-Silva A, Gallego Arias V, Soares L, Martin A, Roberto Marcondes Martins L. Influence of fiber-post translucency on the degree of conversion of a dual-cured resin cement. J Endod 2007;33:303–5.
[211] Teixeira ECN, Teixeira FB, Piasick JR, Thompson JY. An in vitro assessment of prefabricated fiber post systems. J Am Dent Assoc 2006;137:1006–12.
[212] Roberts H, Leonard D, Vandewalle K, Cohen M, Charlton D. The effect of a translucent post on resin composite depth of cure. Dent Mater 2004;20:617–22, http://dx.doi.org/10.1016/j.dental.2003.10.004.
[213] Kim YK, Kim SK, Kim KH, Kwon TY. Degree of conversion of dual-cured resin cement light-cured through three fibre posts within human root canals: an *ex vivo* study. Int Endod J 2009;42:667–74, http://dx.doi.org/10.1111/j.1365-2591.2009.01565.x.
[214] Navarra CO, Goracci C, Breschi L, Vichi A, Corciolani G, Cadenaro M, et al. Influence of post type on degree of conversion of a resin-based luting agent. Am J Dent 2012;25:17–20.
[215] Urapepon S. Degree of conversion of resin composite cured by light through a translucent fiber posts. J Adv Prosthodont 2014;6:194–9, http://dx.doi.org/10.4047/jap.2014.6.3.194.
[216] Özcan M, Zamboni S, Valandro F, Bottino M, Bagis B. Microhardness of dual-polymerized resin cement around a translucent fiber post in the intraradicular environment. J Conserv Dent 2011;14:370–3, http://dx.doi.org/10.4103/0972-0707.87200.
[217] Ferrari M, Breschi L, Grandini S. Fiber posts and endodontically treated teeth: a compendium of scientific and clinical perspectives. Modern Dentistry Media; 2008.
[218] Dauvillier BS, Feilzer AJ, De Gee AJ, Davidson CL. Visco-elastic parameters of dental restorative materials during setting. J Dent Res 2000;79:818–23, http://dx.doi.org/10.1177/00220345000790030601.
[219] Braga R, Boaro L, Kuroe T, Azevedo C, Singer J. Influence of cavity dimensions and their derivatives (volume and 'C' factor) on shrinkage stress development and microleakage of composite restorations. Dent Mater 2006;22:818–23, http://dx.doi.org/10.1016/j.dental.2005.11.010.
[220] Salz U, Bock T. Testing adhesion of direct restoratives to dental hard tissue — a review. J Adhes Dent 2010;12:343–71, http://dx.doi.org/10.3290/j.jad.a19741.
[221] Malhotra N, Kundabala MA. A review of light-curing considerations for resin-based composite materials: Part II. Compend Contin Educ Dent 2010;31:584–8, 590-1; quiz 592, 603.
[222] Malhotra N, Mala K. Light-curing considerations for resin-based composite materials: a review. Part I. Compend Contin Educ Dent 2010;31:498–505, quiz 506, 508.

[223] Rueggeberg FA. State-of-the-art: dental photocuring — a review. Dent Mater 2011;27:39–52, http://dx.doi.org/10.1016/J.DENTAL.2010.10.021.

[224] Price R, Shortall A, Palin W. Contemporary issues in light curing. Oper Dent 2014;39:4–14, http://dx.doi.org/10.2341/13-067-LIT.

[225] Price RB, Ferracane JL, Shortall AC. Light-curing units: a review of what we need to know. J Dent Res 2015;94:1179–86, http://dx.doi.org/10.1177/0022034515594786.

[226] (ISO) ISO. Dentistry — powered polymerization activators (ISO 10650:2018); 2018. https://www.iso.org/obp/ui#iso:std:iso:10650:ed-2:v1:en. (Accessed 22 September 2018).

[227] Strassler HE. Successful light curing — not as easy as it looks. Oral Health 2013;103:18–27.

[228] Strassler HE, Price R. Understanding light curing, Part II. Delivering predictable and successful restorations. Dent Today 2014:1–8, quiz 9.

[229] Ernst C-P, Price RB, Callaway A, Masek A, Schwarm H, Rullmann I, et al. Visible light curing devices — irradiance and use in 302 German dental offices. J Adhes Dent 2018;20:41–55, http://dx.doi.org/10.3290/j.jad.a39881.

[230] Scott BA, Felix CA, Price RBT. Effect of disposable infection control barriers on light output from dental curing lights. J Can Dent Assoc 2004;70:105–10.

[231] McAndrew R, Lynch CD, Pavli M, Bannon A, Milward P. The effect of disposable infection control barriers and physical damage on the power output of light curing units and light curing tips. Br Dent J 2011;210:E12, http://dx.doi.org/10.1038/sj.bdj.2011.312.

[232] Strassler HE, Price R. Understanding light curing, Part I. Delivering predictable and successful restorations. Dent Today 2014;33, 114, 116, 118.

[233] Roberts HW, Vandewalle KS, Berzins DW, Charlton DG. Accuracy of LED and halogen radiometers using different light sources. J Esthet Restor Dent 2006;18:214–22, http://dx.doi.org/10.1111/j.1708-8240.2006.00023.x.

[234] Pilo R, Oelgiesser D, Cardash HS. A survey of output intensity and potential for depth of cure among light-curing units in clinical use. J Dent 1999;27:235–41.

[235] Pires JA, Cvitko E, Denehy GE, Swift EJ. Effects of curing tip distance on light intensity and composite resin microhardness. Quintessence Int (Berl) 1993;24:517–21.

[236] Xu X, Sandras DA, Burgess JO. Shear bond strength with increasing light-guide distance from dentin. J Esthet Restor Dent 2006;18:19–27, discussion 28.

[237] Price RB, Dérand T, Sedarous M, Andreou P, Loney RW. Effect of distance on the power density from two light guides. J Esthet Dent 2000;12:320–7.

[238] Maleknejad F, Ameri H, Manafi S, Chasteen J, Ghavamnasiri M. The effect of photoactivation time and light tip distance on the degree of conversion of light and dual-cured dentin adhesives. Indian J Dent Res 2013;24:225–8, http://dx.doi.org/10.4103/0970-9290.116690.

[239] Maucoski C, Zarpellon DC, dos Santos FA, Lipinski LC, Campagnoli EB, Rueggeberg FA, et al. Analysis of temperature increase in swine gingiva after exposure to a Polywave® LED light curing unit. Dent Mater 2017;33:1266–73, http://dx.doi.org/10.1016/j.dental.2017.07.021.

[240] Price RB, Rueggeberg FA, Labrie D, Felix CM. Irradiance uniformity and distribution from dental light curing units. J Esthet Restor Dent 2010;22:86–101, http://dx.doi.org/10.1111/j.1708-8240.2010.00318.x.

[241] Konerding KL, Heyder M, Kranz S, Guellmar A, Voelpel A, Watts DC, et al. Study of energy transfer by different light curing units into a class III restoration as a function of tilt angle and distance, using a MARC Patient Simulator (PS). Dent Mater 2016;32:676–86, http://dx.doi.org/10.1016/j.dental.2016.02.007.

[242] Zhang C-Y, Yu H, Tong X-W, Cheng H. Effects of cusp inclination and light-curing time on microshear bond strength of a dual-cure, self-adhesive composite cement to zirconia. J Adhes Dent 2018;20:107–12, http://dx.doi.org/10.3290/j.jad.a40298.

[243] Leprince JG, Hadis M, Shortall AC, Ferracane JL, Devaux J, Leloup G, et al. Photoinitiator type and applicability of exposure reciprocity law in filled and unfilled photoactive resins. Dent Mater 2011;27:157–64, http://dx.doi.org/10.1016/j.dental.2010.09.011.

[244] Hadis M, Leprince JG, Shortall AC, Devaux J, Leloup G, Palin WM. High irradiance curing and anomalies of exposure reciprocity law in resin-based materials. J Dent 2011;39:549–57, http://dx.doi.org/10.1016/j.jdent.2011.05.007.

[245] Calheiros FC, Daronch M, Rueggeberg FA, Braga RR. Degree of conversion and mechanical properties of a BisGMA:TEGDMA composite as a function of the applied radiant exposure. J Biomed Mater Res B Appl Biomater 2008;84B:503–9, http://dx.doi.org/10.1002/jbm.b.30897.

[246] Mills RW, Uhl A, Jandt KD. Optical power outputs, spectra and dental composite depths of cure, obtained with blue light emitting diode (LED) and halogen light curing units (LCUs). Br Dent J 2002;193:459–63, discussion 455.

[247] Durey K, Santini A, Miletic V. Pulp chamber temperature rise during curing of resin-based composites with different light-curing units. Prim Dent Care 2008;15:33–8, http://dx.doi.org/10.1308/135576108783328409.

[248] Millen C, Ormond M, Richardson G, Santini A, Miletic V, Kew P. A study of temperature rise in the pulp chamber during composite polymerization with different light-curing units. J Contemp Dent Pract 2007;8:29–37.